OBSERVATIONS ON THE MITOTIC RATE IN STRATIFIED SQUAMOUS EPITHELIUM WITH SPECIAL REFERENCE TO DIURNAL VARIATION

being

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by

Harendra Prasad Sinha, M.B.B.S.
Department of Anatomy
Patna University
Patna, India.

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C O N T E N T S

I N T R O D U C T I O N.

SURVEY OF LITERATURE.

A survey of literature showed that a number of investigators noticed cyclic variations in the average number of mitoses in different tissues of plants and animals corresponding to a 24 hour cycle. These reports indicated that light, habit of the animal, time of feeding, and carbohydrate metabolism might have been responsible for this periodicity.

A number of plants have been studied. Karsten (1915) found that, in Spirogyra, maximum mitotic activity occurred at about mid-night; in Allium, Kellicott (1904) observed two maxima: a primary one at 11 p.m. and a secondary rise at 1 p.m. On the other hand, Stalfelt (1921) noted that mitotic activity in the roots of Picum Sedaticum occurred at 9 to 11 a.m. Furthermore, Berinsohn (1919) stated that allium root tips contained more karyokinetic figures after a period of exposure to darkness than after a similar exposure to light.

In the course of similar investigations, Thuringer (1928) studied the mitotic activity in the epidermis of foreskin of only one infant of 17 days and a boy 3 years old. His "mitotic index" was given as the ratio of mitotic figures observed to the number of cells in 25 serial sections. On the basis of the examination of only one sample of 25 serial sections/

sections from the two children, he stated that mitotic activity was uniformly greater in young individuals than in those of advanced years. He also stressed the importance of 'fixation time' and said that the number of mitotic figures observed was inversely proportional to the delay in 'fixation time' (the time which elapsed between death of the animal and transfer of the tissue to the fixative). This statement had good support in view of the fact that he examined mitotic activity in the foreskin of the two infants fixed instantaneously and subsequently at 5 minute intervals up to 15 minutes and noticed a marked decrease in the number of mitotic figures with increase in the 'fixation time'. Again on the basis of single samples of either 25 or 50 serial sections from the skin of the ear, leg and scalp of different adult persons, he said that the process of regeneration of epidermis was dependent upon physiological requirements of the region from which the tissue was taken and that regeneration progressed faster in some regions than in others. His results showed a higher rate of mitosis in scalp (1 : 2,414) as compared to that in the ear (1 : 268,275) and leg (1 : 378,325). In view of the possible variations in the rate of mitosis due to difference in age, time at which the tissue was taken and individual variation, it has been difficult to attribute much significance to this statement. In examining the sections of the prepuce from the two children, he frequently found aggregations/

aggregations of mitotic figures extending through an average of about 10 serial sections of 10 μ thickness, the largest diameter of these 'growth waves' being approximately 100 μ. According to him, it was possible to count as many as 10 to 14 mitotic figures under high power (X 400) in a single field through the centre of a 'growth wave', while toward the periphery of these proliferation centres the number of mitotic figures tapered off to zero. The above observations with regard to the 'growth wave' clearly required further clarification in view of the very small number and size of the samples used by Thuringer.

Cooper and Schiff (1938) examined the mitotic activity in the prepuce of 13 eight day old infants. Having fixed the tissue in 1% acetic acid for 24 hours they separated the entire layer of epidermis from the dermis and stained with Ehrlich's haematoxylin. 7 samples from 7 different infants were examined at irregular intervals between 7.30 a.m. and 11.40 a.m. and similarly 6 samples from 6 different infants at irregular intervals between 8.45 p.m. and 12.45 a.m. In each sample 5000 cells were counted in successive fields and the number of mitotic figures recorded. They noted that maximum mitotic activity (35 mitotic figures per 5000 cells) occurred at 9.45 p.m. and the minimum (7 mitotic figures per 5000 cells) at 10.25 a.m. No evidence was given for the periods from 11.40 a.m. to 8.45 p.m. and 12.45 a.m. to 7.30 a.m. Moreover they/

they did not give any indication either of the periods of rest and activity or the periods of light and darkness or the time of feeding, though, by inference, the lighting conditions were the natural day and night.

Broders and Dublin (1938), in the course of an examination of 10 μ thick sections of newly born foreskin at one hourly intervals during the 18 hour period from 7 a.m. to 1 a.m., counted two series of 5000 cells in each specimen and noted the number of mitotic figures present. Their mitosis coefficient was "the number of mitotic figures per 1000 cells". They stated that if they were justified in interpreting the mitosis coefficient as an index of mitotic activity, they were led to conclude that mitotic activity was approximately twice as frequent at night as in the day time. The results were based on only one series of observations and there was no mention of the number of sections examined from each specimen and whether sections were taken serially or according to random numbers from the whole length of the foreskin. Due to lack of detailed information regarding the lighting conditions it was not possible to make any correlation between the mitotic activity and onset of light or darkness. However, they stated "it appears that during the day, the emphasis lies on ~~the~~ work, digestion, respiration and other processes of like nature, and during the night, when the need of these functions is diminished, attention is turned toward repairing run down tissues and building new ones."

Similarly/

Similarly in animals, the reports of several investigators showed a marked difference of opinion as to the time at which maximum and minimum mitotic activity occurred.

Fortuyn- van Leijden (1917) studied the mitotic activity in mesentery, cornea, small intestine and liver of six 2 day old kittens killed at about 4 hourly intervals, starting at 7 a.m., in the course of a 24 hour period. 5 μ thick sections were examined from all the tissues except mesentery in which case pieces of mesentery were spread on a slide and stained. It has been stated that she counted a large number of cells together with mitotic figures and found out the percentage of dividing cells. Results from all the tissues except liver showed that maximum cell division occurred at 10.30 p.m.: mesentery, 107 mitotic figures in 9972 cells; cornea, 9 mitotic figures in 3066 cells; small intestine, 127 mitotic figures in 3093 cells and minimum mitosis occurred at 10.30 a.m.: mesentery, no mitotic figures were found; Cornea, 1 mitotic figure in 3167 cells; small intestine, 58 mitotic figures in 3070 cells. Investigations on the liver were not pursued as the number of mitotic figures observed was extremely small. It was noted that different tissues exhibited different rates of mitosis at the same time. The number of observations was small and there was no mention of the body activity and the conditions of temperature and light, though the light was, by inference, the ordinary light of day and night.

In/

In the course of similar investigations on the small intestine of 2 week old mice Fortuyn- van Leijden (1926) found that maximum mitosis (3.4%) occurred at 7 a.m. and 11 a.m. and minimum (1.5%) at 3 a.m. She maintained that in spite of the fact that the animals belonged to different litters and the chances of individual variation were greater in this case, yet there was a suggestion of periodic nuclear division. The lighting conditions and habits of the animals were again not mentioned and the number of observations was small.

Carleton's (1934) observations on mouse skin differed from the findings of Fortuyn- van Leijden (1926). He noticed a daily periodic rhythm with a maximum (1.3% to 1.4%) between 8 p.m. and mid-night and a minimum (0.6%) at mid-day. He thought that the periodic rhythm was caused by the difference in illumination. The results were based on observations on 48 mice killed in groups of six at 4 hourly intervals starting at 12 o'clock in a 24 hour period. The percentage number of mitotic figures was based on a count of 5000 cells, made on 5 different groups of 1000 cells. Although he thought that lighting conditions were important factors in the control of the diurnal rhythm, still he did not mention clearly ~~about~~ the onset and the duration of light and darkness in the diurnal sequence. Age of the animals was a variable factor as he used mice of different ages ranging from 8 hours to 7 days after birth.

Cooper/

Cooper and Franklin (1940), working on mouse epidermis, supported the observations of Fortuyn- van Leijden (1926) and held that the period of maximum mitotic activity occurred at 10 a.m.; the period of minimum mitotic activity at 10 p.m. and that the average number of dividing cells encountered during the day was more than twice as great as during the night. They considered that the occurrence of the peak of mitotic activity during the day in the epidermis of the mouse, in contrast with the condition in man where the greatest mitotic activity was thought to occur during the night, might possibly be explained by the nocturnal habit of the mouse, the period of rest and tissue repair occurring during the day.

Blumenfeld(1939), in studies on the epidermis of 96 adult male albino rats killed in groups of eight at intervals of 2 hours during a period of 24 hours, observed a diurnal periodicity of mitotic activity which was maximum from 8 to 10 a.m. (75 mitotic figures per 1000 high power fields) and minimum from 8 to 10 p.m. (19 mitotic figures per 1000 high power fields). From each specimen he used every 4th section of 8 μ thickness and examined a total of 5000 fields.

In a similar investigation on the renal cortex of the same 96 rats, Blumenfeld (1938) found that the maximum mitosis (59.8 mitotic figures per 1000 high power fields) occurred from 2 to 4 p.m. and minimum (28.5 mitotic figures per 1000 high power fields) from 10 p.m. to mid-night. In this/

this case he mounted every 20th section of 8 μ thickness and examined 250 fields in every 4th section on the slide till 1000 fields were examined.

Again, in the same 96 rats, Blumenfeld (1942) studied the mitotic activity in the sub-maxillary salivary gland and found that the 'average minimal mitotic activity' (11.5 mitotic figures per 500 high power fields) was present between 2 ~~to~~ and 4 a.m. and that there was no special period of maximum mitotic activity. In this case, he examined 500 fields in 8 μ thick serial sections from the gland of each animal.

Blumenfeld thus concluded "whatever the factors that regulate mitosis may be, those immediately concerned with when and how often it occurs act or reside within the organ as a unit."

In a later work, Blumenfeld (1943) studied the mitotic activity in the epidermis of 65 male mice two months old. The technique employed was similar to that used in rats. He found that the maximum mitosis (37.4 mitoses per 500 high power fields) occurred at 12 noon and the minimum (9.1 mitoses per 500 high power fields) at 8 p.m. The character of the curve of mitotic activity during 24 hours was similar to that found in the case of rat epidermis.

Blumenfeld's observations on rats and mice conformed with the observations on mice by Cooper and Franklin (1940) and Fortuyn- van Leijden (1926) but were diametrically opposed to/

to those of Carleton (1934). This conformity was only broadly true in as much as the maximum mitotic activity occurred during the day and minimum during the night. While it was true that Blumenfeld studied 1000 fields, these only represented the examination of 4 to 5 sections from the whole organ. Moreover, there was no mention of the temperature conditions, length of day and night, activity of the animal and whether food was always available or feeding was at definite times. Observations taken from animals killed at the same hour exhibited enormous individual variation.

In the course of further research on albino rats Blumenfeld (1944) found that there was a diurnal variation in the volume of urine excreted and the weight of the food eaten. At the same time, he found that there was no diurnal variation in the weight of the solid content of the urine. At a given time, the rate of mitosis in the renal cortex varied inversely with the volume of urine excreted during the preceding 6 hours and the mitotic activity in the submaxillary salivary gland varied inversely with the amount of food eaten during the preceding 6 hours. These data, according to him, furnished a factual basis for the view that 'function restrained growth'. These conclusions were scarcely justifiable in view of the fact that the time during which the food was eaten or the urine excreted, was different from that at which the mitotic activity was studied. In addition, with regard to his/

his experiments on the renal cortex, he assumed that a large volume of urine (low concentration) indicated more work done by the cells in the tubular epithelium and a small volume of urine (high concentration) indicated less work done by those cells. This, in fact, was contrary to what would be expected under those circumstances.

Bullough (1947), in the course of his extensive research, took all possible precautions to avoid factors which were liable to cause error in the result except that he took samples which consisted of serial sections and not according to random numbers. However, he determined the diurnal cycle of mitosis in the ear epidermis of adult male mice by removing small pieces of ear from the same group of mice at 2 hourly intervals throughout a period of 24 hours. The mice used were between 3 and 4 months old. A considerable degree of individual variation was found but on the average the maximum mitotic activity was at 06.00 hours and 14.00 hours and the minimum mitotic activity at 10.00 and 20.00 hours. These observations were confirmed by killing groups of mice, each group consisting of five males, at the same 2 hourly intervals throughout 24 hours. Similar variations in the mitotic activity of the ear epidermis were observed and, in addition, similar cycles were evident in the mid-dorsal epidermis of the back, stratified epithelium of the oesophagus, the lining epithelium of epididymis and the proliferating/

proliferating zone of duodenal mucosa. In the last tissue the rate of cell division never fell to a very low figure and in the proliferating centres of the intestinal lymph nodes, as well as in seminiferous tubules of the testes, there was no trace of a cycle and the rate of cell division remained constantly high.

With the help of a special cage Bullough (1947) studied the spontaneous body activity of the mouse throughout 24 hours. Hourly records of the activity were noted for two weeks and the average activity per hour was then determined. By comparing the average figures so obtained with the average figures of the mitotic activity, Bullough made the significant correlation that when the animals were at rest mitotic activity was at a maximum and that when they were awake and active it was at a minimum. According to his graphs this correlation was not striking at one point where the rise in the body activity between 06.00 and 08.00 hours was very small but coincided with a very significant fall in the mitotic activity in the epidermis of the mouse. However, he stated that this correlation permitted an explanation of the individual variation in mitotic activity, since there was also a high degree of individual variation in spontaneous body activity. He maintained that it also permitted an explanation of the contradictory results which have been reported in the past regarding mitotic rhythm in the mouse, since it was evident/

evident that the rhythm of the body activity must have been strongly affected by difference in age, sex, condition of the animals used, season of the year and the time of feeding.

In order to carry out further investigations on the relationship between the body activity and mitotic activity Bullough (1947) studied the effects of rest, experimentally induced by the injection of an optimum dose of 'somnifaine' and exercise (forced) in a revolving cage, on the epidermal mitotic activity of the adult male mouse. He found that the mitotic activity and the body activity were inversely related to each other and stated, "The conclusion is now justified that the rate of epidermal mitosis normally increases during sleep and decreases during hours of wakefulness and exercise. In this way, the form of diurnal mitosis cycle is determined by the habits of the animals."

Bullough (1948) found that a relation existed between the mitotic activity and the blood sugar and that an increase in the blood sugar level, induced by a subcutaneous injection of 20 mg. of starch in 0.9% saline, resulted in an increased mitotic rate. Conversely, a decrease in the blood sugar level, induced by insulin, caused a decreased mitotic rate and a deep mitotic depression was caused by an injection of phloridzin. In the normal animals he found that the diurnal changes in the blood sugar level were the inverse of the diurnal changes in mitotic activity, the concentration of the/

the blood sugar being relatively low during sleep when the rate of mitosis was relatively high. Therefore he concluded that the level of blood sugar as such was not an important factor in the control of the diurnal mitotic cycles and suggested, without direct evidence, that probably the critical factor in the control of these cycles was the concentration of sugar, or glycogen within the tissues themselves.

Bullough and Eisa (1950), in the course of their research on the glycogen content in the following tissues, found that it was maximum at 14.00 hours, in liver (1211 mgm. glucose per 100 g. fresh tissue) and in skin (80 mgm. glucose per 100 g. fresh tissue) and minimum, in liver (788 mgm. glucose per 100 g. fresh tissue) and in skin (50 mgm. glucose per 100 g. fresh tissue) at 22.00 and 20.00 hours respectively. They noticed that the concentration of tissue glycogen was highest when the animals were asleep and lowest while they were awake and active. On the basis of these observations and others, already referred to, they stated, "These results, together with others previously reported, are in agreement with the theory that at the onset of sleep, glucose is deposited from the blood into the tissues where it appears in the form of glycogen. Since it is known that glucose, or glycogen, is a critical substance affecting mitotic activity in the adult mouse, it is logical to find that/

that an increase in the epidermal glycogen content is accompanied by a greatly increased mitosis rate. On waking, the reverse process takes place, glycogen being withdrawn as glucose in the blood and mitotic activity falling to a low level."

Laws (1952) stated that, in tumor bearing mice, when the mitotic activity fell, the blood sugar level during that period remained unchanged. This led him to think it unlikely that the depression of mitosis which developed progressively in the epidermis of tumor bearing mouse, could be attributed to any inadequacy in the supply of carbohydrate to these cells. These observations, quite different from those of Bullough (1948), were taken from a group of diseased mice, a factor which might have been responsible for the difference in the result.

With regard to the relationship between the blood sugar level of the mother and the foetus, Huggett (1954) stated that in rodents glucose passed very freely across the placenta to the foetus after an intravenous injection of glucose to the mother. He further said that when fructose reached the foetus, it increased the glucose content, suggesting that the foetus could transform it to glucose, possibly in the liver.

Investigations on the relationship between mitotic activity and age, sex, diet, temperature, shock, stress, colchicine/

colchicine injection and lighting conditions have been carried out by various workers.

AGE: Loeb and Haven (1929) stated that mitotic activity in the epidermis of very young, sexually immature guineapigs was lower than in the case of adults and that there was a gradual decrease in the proliferative activity in the adult guineapigs with increasing weight and age. In the course of this work no attention was paid to the time and the exact age at which the animals were sacrificed and there was no mention about the standard deviation of the values obtained. As the results stand, it has been impossible to say how far they could be relied upon.

Ortiz Picon (1933) said that, in the case of the epidermis of white mouse, the mitotic rate reached its highest level soon after birth and decreased quickly in the course of a few weeks to a minimum activity at the age of one month, which coincided with the commencement of puberty. From this time onwards, the mitotic activity slowly increased until the age of 6 to 9 months followed by a steady decrease until the advent of old age, during which the number of mitoses did not undergo any change. Ortiz Picon did not consider the possibility of variations due to individual variation and difference in sex which have been reported (see later) to have an influence on the mitotic activity.

Bullough (1949), in the course of a study of the mitotic/

mitotic activity in each month of the life of the mouse, examined a skin sample taken at 2 hourly intervals between 08.00 and 20.00 hours and thus followed half the diurnal cycle of mitotic activity. He expressed the results as the number of mitoses per unit section length of 1 cm. of skin. He observed that during the immature phase (birth to 3 months), the peak of mitosis was at 14.00 hours and that the highest number of mitoses observed per unit section length of 1 cm. was only 5. Further, he noticed that the total of the average numbers of mitoses observed during a 12 hour period was 22. During the mature period (3 months to 12 months), the peak remained at 14.00 hours; the highest number of mitoses observed per unit section length of 1 cm. was 8 and the total of the average numbers of mitoses observed during a 12 hour period was 30. During middle age (13 to 18 months), in the Strong's CBA strain and not Kreyberg's strain, the peak of mitosis gradually shifted to 08.00 hours towards the end of the period; the highest number of mitoses observed per unit section length of 1 cm. rose to 14 and the total of the average numbers of mitoses observed during a 12 hour period rose to 47. During senility (19 months to death), the peak of mitosis returned to 14.00 hours; the highest number of mitoses observed per unit section length of 1 cm. was only 5 and the total of the average numbers of mitoses observed during a 12 hour period was 18. The mice of Strong's/

Strong's CBA as well as Kreyberg's strain showed similar variations at different stages of life except that the shift in the peak during the middle age occured in Strong's CBA strain only.

In addition to the apparent increase in the rate of mitosis and the shift of the peak with advancing age, Bullough also noticed, in the course of the complete cycle (extending throughout 24 hours) in the mice of the Strong's CBA strain, that the immature mice showed periods of maximum mitotic activity at: 04.00 hours (5.6 mitoses per unit length), 08.00 hours (4.2 mitoses per unit length) and 14.00 hours (5.8 mitoses per unit length) and the periods of minimum mitotic activity occurred at: 06.00 hours (1.6 mitoses per unit length), 10.00 hours (1.4 mitoses per unit length), and 22.00 hours (1.5 mitoses per unit length); mature mice showed 2 peaks at 06.00 hours (9.1 mitoses per unit length) and 14.00 hours (8.6 mitoses per unit length) and two periods of minimum mitotic activity at 10.00 hours (2.7 mitoses per unit length) and 20.00 hours (2.2 mitoses per unit length); middle aged mice also showed 2 peaks at 08.00 hours (15.3 mitoses per unit length) and 24.00 hours (14.8 mitoses per unit length). To ascertain whether the increase in the mitotic activity with advancing age was real or was due to an increase in the time required for each mitosis to be completed in advanced age, thus causing more mitotic/

mitotic figures to be observed, Bullough used colchicine to arrest all mitoses at metaphase and observed that there was evident increase and decrease in the rate of mitosis in the approximate proportions of immature, 1; mature, 2; middle age, 3; and senile, 1.

Teir, Schauman and Sundell (1952) stated that, in the gastric mucosa of the youngest rats (some hours old), the mitotic ratio was fairly low (2.8 mitoses per 1000 cells) and at 2 to 3 weeks the highest mitotic ratio was 7.2 mitoses per 1000 cells. Until the age of two months, the mitotic ratio remained high and after the 2nd month it began to decrease gradually till 2 years, when the mitotic ratio fell to 1 mitoses per 1000 cells. In spite of the reported diurnal variation in the mitotic activity and variation during the oestrous cycle, these workers used animals without reference to sex and killed them at different hours of day and night.

SEX: Loeb and Haven (1929) observed that in the skin of the female guineapig, during the period of oestrous, the mitotic activity was 1.80 mitoses per 1000 cells, a little more than one third of the number occurring in the normal adult male. The rate of mitosis, during the period from the 1st to the 5th day (inclusive) following oestrous, was 2.45 mitoses per 1000 cells, slightly above that found during ~~the~~ oestrous; six days after the oestrous when the corpus luteum was in full activity, the rate of mitosis was 2.14 mitoses per/

per 1000 cells. Seven to ten days after oestrous the rate of mitosis (3.18 mitoses per 1000 cells) was still below the average for normal adult males but was higher than the averages in the earlier periods of heat. Twelve to fourteen days after oestrous, the rate of mitosis was 2.19 mitoses per 1000 cells, while fifteen to sixteen days after oestrous, there was evidence of degeneration in the corpus luteum and the rate of mitosis was 3.78 mitoses per 1000 cells. Thus Loeb and Haven concluded that the average proliferative activity of skin in female guineapigs was diminished as compared with the average proliferative activity in male guineapigs of corresponding weight and age. This diminution affected the follicular as well as the luteal phase of the cycle. The activity rose again toward the end of the cycle, at a time when a new cycle was in preparation and when neither follicular nor luteal substance was active.

Bullough (1942) found, in the skin of the anterior dorsal region of the female mouse, that the peak of mitosis (548 mitoses per 3 mm. section length of skin) occurred during pro-oestrous after which there was a slight decrease during pre-ovulation oestrous, followed by a sudden drop (129 mitoses per 3 mm. section length of skin) after ovulation. A slight rise in met-oestrous preceded a period of very low mitotic activity (89 mitoses per 3 mm. section length of skin) during the 1st day of di-oestrous, after which mitosis gradually increased throughout the 2nd and the 3rd days of di-oestrous/

di-oestrous to be followed once more by a sudden rise in mitotic activity in pro-oestrous. There was no mention about the time of ~~the~~ day at which the animals were killed, although by inference it was most likely constant.

Bullough (1948) observed, in the ear epidermis of the female mouse, that the peak in the mitotic activity occurred on the 3rd day of di-oestrous and again in early oestrous, and that the minimum occurred on the 1st day of di-oestrous and again in pro-oestrous. During all stages of the sexual cycle, the diurnal variation in mitotic activity was present.

DIET: Rabinovitch (1928) found, in a study of the mitotic activity in thyroid epithelium, that of 12 guineapigs underfed in terms of quantity for 10 days (weight lost was 25% of the normal weight) eleven failed to show any mitoses at all, and in one remaining animal the number of mitoses observed was slightly less than the average number of mitoses in the normal animals. There was, however, no mention of the time at which the animals were killed.

Loeb, Haven, Genther and Friedman (1930) stated that underfeeding tended to decrease the mitotic activity of the ear epidermis of guineapigs but that this change was not accomplished very readily, for it might be resisted in individual cases for a considerable period of time. The effect of underfeeding on the mitotic activity, observed by these workers,/

workers, was not striking and the results were very variable. So much so that in some of the underfed animals they actually noticed an increase in the rate of mitosis. This variability in the result might have been due either to individual variation or differences in the age of the animals or differences in hours at which the animals were killed or differences in sex or difference in the number of days for which the animals were underfed.

The statement of Bullough (1949) supported the observations of Rabinovitch (1928) because Bullough also noticed that starvation had a powerful effect in depressing epidermal mitosis in mice, so much so that after 36 hours such activity was almost entirely eliminated. He found that a similar effect was produced by restricted diets. Animals, rationed to 66% of the normal amount of food, had an epidermal mitotic rate which was less than 40% of that of well fed controls. If rationed to 50%, the mitotic rate dropped to about 15% of that of the controls.

Blumenthal (1940), working on the adrenal cortex of guineapigs, observed "the rise in mitotic activity seems to occur irrespective of the time of the day when the feeding takes place. It is probably due to metabolic processes which are initiated by the intake of food. There is no indication in these experiments that light plays a part in the determination of rhythmic mitotic activity; but further studies/

studies are necessary to determine whether it may not be a subsidiary factor." In the course of his work he fed different animals at different hours of day and night and found that in all the cases the peak of mitotic activity in adrenal and thyroid glands occurred between 4 and 12 hours after feeding. Thus, peaks of mitotic activity were found throughout the 24 hours depending upon the time of feeding.

TEMPERATURE: Loeb and Haven (1929) studied the effect of environmental temperature on the mitotic activity in the epidermis of guineapigs. They stated that there was in general a tendency towards diminished proliferative activity of cells during the summer months. The difference in the average rate of mitosis during winter and summer months, as noticed by them, was very slight. This slight difference could be due to the fact that they used animals of different age and sacrificed them at different times of day.

Bullough (1950) recorded the body temperature of mice at 2 hourly intervals throughout a 24 hour period along with the rate of mitosis in the skin of those animals and stated that a general inverse relationship was evident between the two graphs, the lower body temperature (35.2 degrees centigrade) of the sleeping animals coinciding with high mitotic activity (7.6 mitoses per unit section length of 1 cm. skin) and the high body temperature (37.7 degrees centigrade) of waking animals coinciding with low mitotic activity (1.7 mitoses/

mitoses per unit section length of 1 cm.). On the other hand he noticed that an artificial reduction of body temperature of a waking mouse to a level typical of sleep was not followed by a rise in the mitotic activity and similarly the artificial prevention of a drop in the body temperature of a sleeping animal did not interfere with the normal rise in the mitotic activity which took place at this time. The only significant result noted by him was that a reduction in the mitotic activity occurred in mice which were kept at a low environmental temperature (0 degrees centigrade).

OTHER FACTORS: Bullough and Green (1949) noticed a striking influence of shock on the mitotic activity in ear skin of the mouse. They stated that in animals suffering from ischaemic shock, produced by the application of a tourniquet to the upper part of the hind limb, the mitotic rate rapidly fell to zero, $1\frac{1}{2}$ hours after removal of the tourniquet.

A similar depression in epidermal mitosis in mice in conditions of stress was noticed by Bullough (1952) in the course of his study of the mitotic rate in animals kept in a crowded cage.

Investigations on the effects of Colchicine injection on the rate of mitosis by Bullough (1949) showed that Colchicine inhibited mitosis in or after the metaphase for a period of 5 hours after the injection, following which severe nervous depression occurred which ended in the death of some of/

of the animals.

In a series of researches on factors which affect mitotic activity in the mouse, Bullough (1950) found that the injection of carbohydrate stimulated epidermal mitosis and he was able to use the consequent wave of cell division to estimate the time occupied by these cells in mitosis. He stated that in the ear epithelium, it took 120 to 180 minutes for the whole process of actual cell division; in cells of the spleen, prophase - 20 to 30 minutes, metaphase - 6 to 15 minutes, anaphase - 8 to 14 minutes, telophase - 9 to 26 minutes and the total time taken varied from 43 to 90 minutes.

Fell and Huges (1949) found that of seventeen intermitotic periods measured in a film record of the growth of one culture of mouse spleen, the range was between 8 and 18 hours.

LIGHT: Fortuyn- van Leijden (1926) found that in the root tips of Allium Cepa maintained in constant darkness there existed a rhythmical cell division with alternating maxima and minima. Illumination during day time changed this rhythm into a daily period with the largest number of mitoses during the period of darkness.

Karsten (1915-18) in his work on root tips and growing buds of various plants found that: (1) continuous exposure to electric light eliminated the periodicity and inhibited growth, (2) illumination with an electric lamp at night,/

night, with darkness by day, gave two maxima instead of one with a time interval of 12 hours. These observations led him to suggest that there were two warring factors, firstly, an inheritence factor from parents accustomed to the natural diurnal variation of light, and secondly, a direct adaptation to the changed conditions of light.

Carleton's (1934) observations on mice showed that the periodicity, already referred to, was eliminated by continuous exposure to light; continuous darkness did not affect the normal diurnal periodicity. Exposure to light from 12 noon to 12 o'clock at night destroyed the periodicity completely whereas illumination from midnight to midday caused considerable irregularity and eliminated the periodicity. Carleton however used animals of different ages and the period (10 days), during which the animals were kept under altered conditions, was short. Finally, there was no mention whether the animals had become accustomed to the changed lighting conditions before they were sacrificed.

In investigations on the mechanism of the regulation of the mitotic activity, Blumenfeld (1944) kept a group of 22 rats in a completely dark room from 8 a.m. to 8 p.m. and in a brightly illuminated room from 8 p.m. to 8 a.m. for a total period of 48 hours. From the results of his experiments extending for 48 hours only, he concluded that altering light and dark periods did not change the periodicity of the mitotic/

mitotic activity.

Blumenthal (1940) maintained, as mentioned previously, that a rise in the mitotic activity might occur at any time of the day and night, depending upon the time of feeding and subsequent increase in the metabolic activity, and that lighting conditions did not seem to regulate the periodicity.

OBJECTIVES OF THE PRESENT WORK.

In view of the different findings, reported by the previous workers, regarding the diurnal variation in the mitotic activity in the tissues of animals and human beings and the factors related to it, attempts have been made, in present work, to study the mitotic activity in the oesophageal epithelium of the rat with a view to clarifying some of the differences of opinion. The findings discussed here are the results of observations on: (1) the mitotic activity, in the squamous epithelium of the oesophagus, and the body activity of the rat with special reference to diurnal variation and the relationship of the mitotic activity to the lighting conditions, (2) the mitotic activity in the squamous epithelium of 20 day old foetuses and its relationship to that of the mothers.

MATERIAL AND METHODS

Normal male rats of the Wistar strain were studied. The material was collected during a period of approximately 16 months, and the observations made upon it were therefore taken from animals killed at all seasons of the year. However, apart from the unavoidable variations in the length of the day, conditions were kept as uniform as possible. The times of the day recorded in the various experiments represent Greenwich mean time.

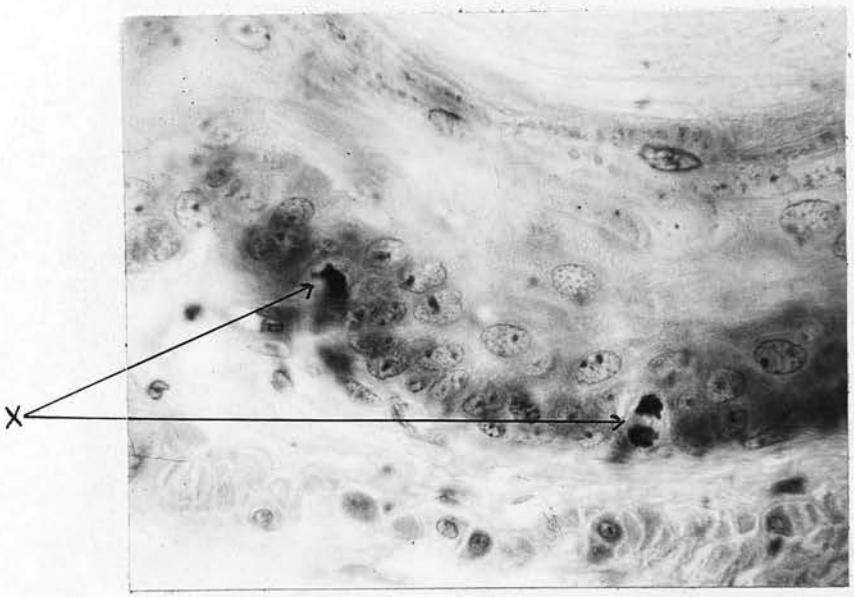
The animals were kept in the animal room under standard conditions of temperature, food and water. The temperature of the animal room was recorded in the morning and in the evening and it was so manipulated by means of an electric radiator that the temperature always remained between 66°F and 76°F. The animals were fed daily at 09.00 and 17.00 hours in quantities sufficient to ensure that food and water was always available to the animals throughout the 24 hours. The age of the rats was between 120 and 130 days at the time of sacrifice. At first, the weight of every rat was recorded each week with the idea that they would attain some constant weight in adult life and indicate the end of the growth period. It was noticed that the weight continued to increase and therefore this step was abandoned, all the animals being sacrificed at the above age. To avoid error due/

due to possible influence of gas or any chemical substance upon the mitotic activity, it was decided to kill the animals by striking on the head. The rats were tame and did not show signs of fear or excitement at the time when they were handled for sacrifice.

The pinna of the right ear of the rat was immediately removed (in toto) and kept in the Zenker's fixative (25 c.c.) to which 1.25 c.c. of glacial acetic acid was added. Immediately afterwards the cervical and the thoracic regions were dissected carefully and the oesophagus was exposed by splitting the sternum and retracting the trachea to the right side. The whole length of the oesophagus was removed and kept in the fixative along with the pinna. The time taken between the death of the animal and transfer of the tissues to the fixative was never more than 8 minutes. The tissues were kept in the fixative for 20 to 24 hours, after which they were dehydrated in ascending grades of alcohol starting with iodised 70% alcohol, to remove mercuric chloride crystals from the tissues. Finally they were cleared in benzene, embedded in paraffin and sectioned at 10 μ.

Oesophagus

All the blocks were cut in the transverse plane and sections were obtained from the whole length of the oesophagus according to random sample numbers. The same random numbers were used throughout the whole work. Every sample formed/



X800

X Photomicrograph ~~Microphotograph~~ showing the mitotic figures in the Squamous epithelium of the oesophagus of the rat.

formed a true representative of the particular oesophagus and the possibility of an error, due to some special distribution of mitotic activity, was eliminated. After the sections were mounted, dewaxed in xylol and passed through descending grades of alcohol, they were put in 70% iodised alcohol for half an hour in order to remove the excess of mercuric chloride crystals, followed by treatment with saturated solution of hypo for 15 minutes ~~for removing~~ to remove excess of iodine. Having washed with tap water, they were kept in hydrogen peroxide (20 vols.) for 24 hours to bleach the melanin pigments, washed with tap water, kept in 4% iron alum solution overnight followed by treatment with Heidenhain's haematoxylin for 3 hours. Finally they were differentiated with a saturated solution of picric acid in absolute alcohol. Mitotic figures stood out distinctly black against the dull white background of the surrounding tissue.

All mitotic figures were counted in every section and no attempt was made to differentiate the various stages of mitosis. Next, the sections were projected on paper and the outline of the epithelium drawn. Magnification was kept constant at 185 (linear). The area of the magnified epithelium was measured in square centimetres by means of Polar-planimeter and, in most cases, was found to approximate to 50 sq.cm. It was decided, therefore, to adjust the number of mitoses in every section to the number per $50/185^2$ sq.cm. This/

This area ($50/185^2$ sq.cm.) of epithelium was considered as the unit area for expressing the results. In this way, the observed number of mitoses in each section had to be altered very slightly when all the figures were adjusted and no statistically significant error was introduced. The adjustment of the number of the mitotic figures to the number in the unit area was necessary for two reasons, (1) for the sake of comparison, the index of expressing the results had to be the same in all cases, (2) actual experimental counts were to be least disturbed by way of adjustment for they conformed quite well to a known type of distribution, "Poisson distribution". One typical feature of this kind of distribution is that the mean and the variance are in theory the same and in practice not greatly different. In addition, the mitotic activity was also expressed as the number of mitotic figures per section (10 μ) of the oesophagus.

Skin

All the blocks were cut at 10 μ through a plane at right angles to the long axis (apex to the root) of the pinna and sections were obtained from the whole length of the pinna according to random numbers. After mounting the sections, each one was cut transversely by means of a safety razor blade into 7 to 10 parts (segments) to facilitate its projection for drawing purposes. These segments were roughly equal to each other. Staining was done as in the case of the oesophagus./

oesophagus. Before starting the examination of every sample, the number of segments in a single section was determined which yielded approximately $50/185^2$ sq.cm. of epithelium. Then the same number of segments were examined in all sections of the particular sample and all mitotic figures were counted. The epithelium, in and immediately adjacent to the hair follicle, was not included in the examination in view of the possibility that growth of the hair might influence the mitotic activity. The segments of the sections were then projected on paper at known magnification (185 linear) and the area of the magnified epithelium measured in square centimetres by Polar-planimeter. The mitotic activity was thus expressed as the number of mitoses per $50/185^2$ sq.cm. and this area ($50/185^2$ sq.cm.) of epithelium was used as the unit area for expressing the results.

Sampling of the tissue

At first, one rat was sacrificed at 10.00 hours and a sample of 45 sections of oesophagus was selected arbitrarily for examination. Sections included in this sample were obtained according to random numbers from a complete series of sections from the whole length of the oesophagus. The random numbers were obtained from the statistical tables by Fisher and Yates (1952). It was hoped that in this way, variation in the result due to irregular distribution of mitotic activity could be eliminated. The next problem was about/

about the size of the sample, that is, whether the number of sections included in the sample was to be increased or decreased.

The average rate of mitosis in the oesophagus was determined from the above sample taken at 10.00 hours and the standard deviation computed, the values of which were 17.7 mitoses per unit area and 3.5 respectively. The problem was this: (1) How precise was that mean? That is, how much would it be likely to vary if another, equally random sample was taken? (2) What would be the standard deviation of the means if repeated samples were used?

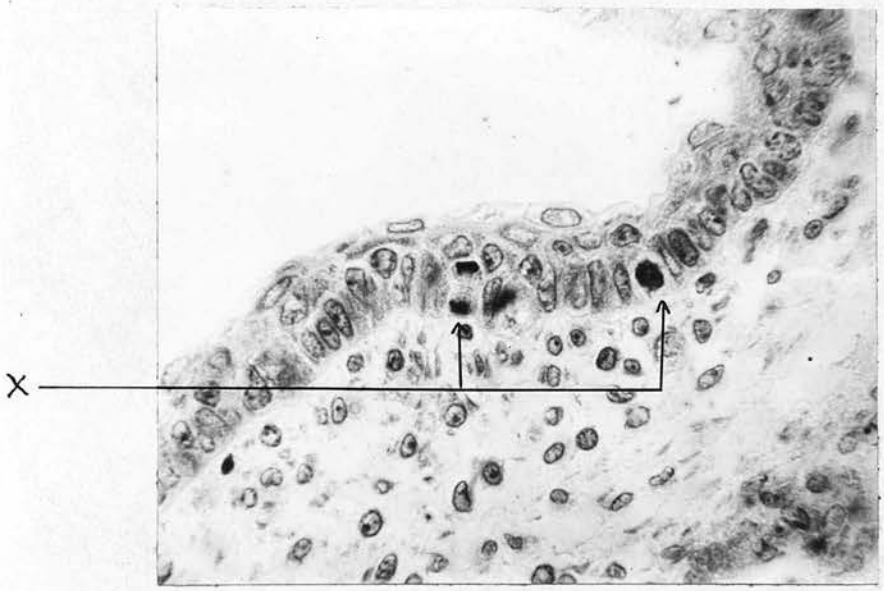
It was known that the standard deviation of means of samples was equal to the standard deviation of ~~the~~ individual sections from every oesophagus in all the rats of Wistar strain sampled, divided by the square-root of the number of sections included in the sample, and is written as $\frac{\sigma}{\sqrt{n}}$. The mean of a sample might well differ from the true mean by as much as twice $\frac{\sigma}{\sqrt{n}}$. It was not likely to differ by more than that amount, that is, the observed mean was likely to lie within the range $X \pm 2(\frac{\sigma}{\sqrt{n}})$ where X was the true mean. Clearly, however, the value of σ was not known and as an estimate of it, the standard deviation of the mean value in the present sample was used. It must be observed that this was however only an estimate, for just as the mean varied from sample to sample, so also would the standard deviation./

deviation. But the latter would vary to a lesser extent and so long as the sample was fairly large the estimate would be a reasonable one and unlikely to lead to any serious error. Thus, with reference to the standard deviation in the present sample, the standard deviation of means in samples of 45 sections would be $3.5/\sqrt{45} = 0.5$.

In conclusion, it might be said that the observed mean might differ from the true mean by as much as 2(0.5). The mean in such a sample that differed from the true mean by more than twice the standard deviation would be a rare event and that which differed from the true mean by more than three times that standard deviation would be a very rare event. It was therefore decided to take 50 sections in all the subsequent samples because even with 45 sections in a sample the observed mean was not likely to differ very much from the true mean.

Foetuses

Foetuses aged 20 days were obtained from normal female rats, in which oestrous had been determined by means of the vaginal smear technique and in which copulation had occurred at a known time of the day. In the case of foetuses that were to be obtained in the forenoon and the afternoon, the female rats were mated at the corresponding time of the day where as in the case of those foetuses that were obtained in the early and the later part of the night, the/



X800

X Photomicrograph ~~Microphotograph~~ showing the mitotic figures in the Squamous epithelium of the oesophagus of the rat foetus.

the female rats were mated in the early part of the night only. Time allowed for copulation was 2 hours. Since the variation in the age by a few hours was not likely to affect the mitotic activity and it was not possible to determine the exact age of the foetus in terms of hours, no effort was made to be very exact regarding the time of mating. Pregnant female rats were killed by striking on the head and foetuses, removed from the uterus, were immediately divided by passing a sharp blade just in front of and behind the fore limbs. The middle piece that contained the oesophagus was placed in the Bouin's fixative for 24 hours, dehydrated in ascending grades of alcohol starting with 70%, cleared in benzene and embedded in paraffin. The oesophagus of the mother was also removed and treated as in the case of the other adult rats. All the blocks were cut transversely at 10 μ and a sample of 25 sections was obtained arbitrarily from each foetus according to random sample numbers. The sections were stained with Heidenhain's haematoxylin and differentiated by saturated solution of picric acid in absolute alcohol. The variation in the area of the epithelium in sections from different foetuses appeared to be too small to cause any significant variation in the mitotic activity. Therefore mitotic activity was expressed as the number of mitoses per section.

Activity Cage

A special wooden cage was used to measure the spontaneous/

spontaneous activity of the rats. The floor of the cage, made of light wood, was in two segments of equal size, each supported but swinging freely on a metal rod passing below its centre of gravity and through the walls of the cage. Each segment of the floor was free from the walls of the cage and moved in a sea-saw manner around the axis of the rod.

Each segment of the floor was connected in series with an electric counter and a separate electric circuit was established for each segment. A brass piece was fixed to the under surface of each segment at the two ends of their anterior borders. At a slightly lower level, a bolt was fixed to the wall of the cage corresponding to the position of each brass piece. One brass piece and the corresponding bolt of each segment formed part of an electric circuit whereas the other bolts served only as a support to those ends of the two segments. The current was taken from the Mains to a transformer-rectifier unit which delivered 50 volts D.C. through the contacts formed by the brass pieces and bolts in the cage to solenoid counters arranged in series with each floor element, the movement of which, by making and breaking the current, activated the counters. In this way, with minimal change in position of the floor, each movement of a rat from one side to the other of either rod was recorded.

Two rats were kept at a time in this experimental cage/

cage and an interval of 10 days was allowed for them to become accustomed to the new environment. From the 11th day onwards records of the body activity were taken for 10 days. For each pair of rats, hourly records were taken daily during the day and once during the night. On other nights, a total record was taken and an average per hour determined.

Experimental Procedure

Control Group: This group consisted of 3 series, each of 12 rats. The 24 rats of series I and II were kept under normal conditions of natural day and night. Two pairs of rats from each series were used for measuring the body activity. It was recorded from the 11th day onwards but the observations were taken only when the pattern of the activity remained similar on every day. Although the pattern of the body activity in the course of 24 hours became constant, the variation in the day to day observation at any given time was noticed to be very great. Therefore an average hourly body activity during the day was calculated from the observations collected during a period of 10 days. With regard to the average hourly body activity at night, an average of the two sets of observations, one from each pair of rats, was determined. Finally all the rats of these two series were sacrificed, two at every 2-hour interval, throughout a single 24-hour period. Rats of series III were kept under conditions where the day light was replaced by artificial light for 80

to/

to 90 days. A dark room was used for this purpose. It was illuminated during the day by a bulb (60 watt) fixed in the wall at a distance of 12 feet from the cage. The inside of the cages received direct light from the source of illumination. The animals were fed at 09.00 and 17.00 hours without causing any disturbance to them. The activity of 4 rats of this series was recorded and animals sacrificed in the same manner as those of series I and II.

Reversed Group: This group consisted of series IV and V. Series IV comprised 12 rats and series V six rats. All the rats of both series were kept under reversed lighting conditions of artificial day and night for 80 to 90 days. The room was kept dark during the day and illuminated during the night. ~~Record~~ Recordings of the body activity and sacrifice of the animals were carried out as in the case of the control group except that the animals of series V were killed at 4-hourly intervals.

Foetus Group: Six foetuses were removed from each pregnant rat, killed at 3-hourly intervals in a 24-hour period. Since 25 sections were examined from each foetus, a total of 150 sections formed the individual samples except in one case where the sample consisted of 100 sections as only 4 foetuses were available. The average mitotic activity for each sample was then determined. Similarly, the average mitotic activity was studied in the oesophagus of the 8 mothers,/

mothers, each naturally corresponding exactly in time to one foetal sample.

Individual Variation Group:

(a) A group of 12 rats, 120 days old, were sacrificed at a time when a high rate of mitosis was expected. A random sample consisting of 50 sections from each rat was examined and the mitotic activity expressed as number of mitoses per section. The mean and standard deviation of these figures were ascertained for each rat. The grand mean and the standard deviation of 12 means was then calculated to show the presence or absence of chances of variation in the results due to individual variation, under natural lighting conditions.

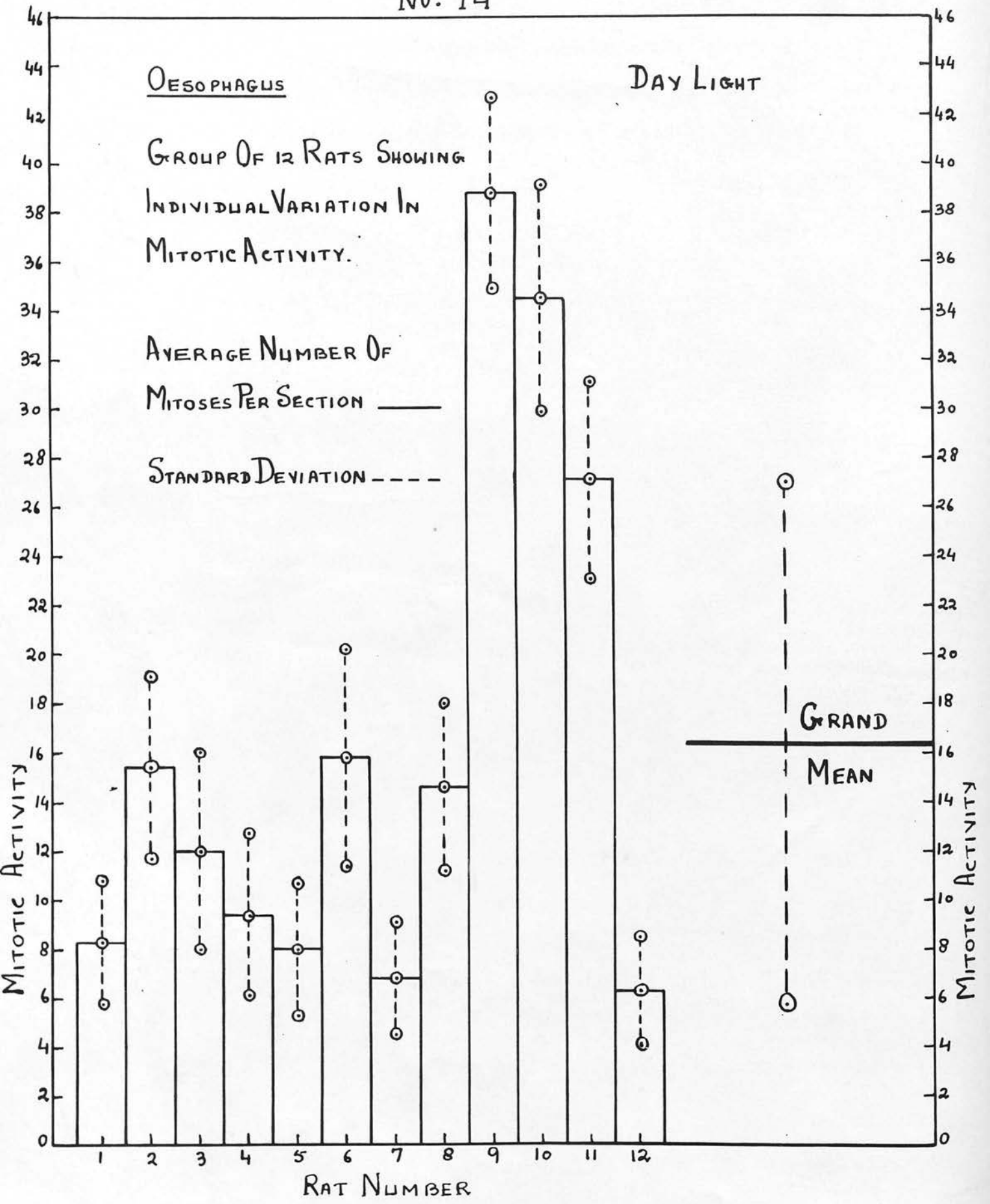
(b) Similarly 6 rats, kept under artificial lighting conditions, were sacrificed at a time when a high rate of mitosis was expected. The average mitotic activity together with the standard deviation was determined for each rat in the manner mentioned above.

Statistical Analysis: The mean value, standard deviation and variance were calculated for each sample in all the groups. To test for the probable significance of variation in the mitotic activity, in the control as well as reversed group, in the course of the 24 hours, the test of significance was carried out and in each series the value of 't' was found with regard to the maximum and minimum rates of mitosis.

The/

The significance of the variation in the mitotic activity was then found by looking up probability tables of the value of 't' corresponding to the "degrees of freedom" present.

NO: 14


OESOPHAGUS
DAY LIGHT
GROUP OF 12 RATS SHOWING INDIVIDUAL VARIATION IN MITOTIC ACTIVITY.
AVERAGE NUMBER OF MITOSES PER SECTION
STANDARD DEVIATION
GRAND MEAN
MITOTIC ACTIVITY
RAT NUMBER
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46
1 2 3 4 5 6 7 8 9 10 11 12

O B S E R V A T I O N S

INDIVIDUAL VARIATION GROUP

(Natural Lighting Conditions)

A group of 12 rats was sacrificed between 10.00 and 11.00 hours, a time at which a high rate of mitosis was expected. The average number of mitoses per section was determined for all the 12 rats; vide table no: 1 and graph no: 14.

The mean values of the individual samples showed an enormous range of variation of mitotic activity, extending from 6.3 to 38.8 mitoses per section. On the basis of this observation, it was not possible to assign any particular hour, in the course of 24 hours, to be the time of the highest or the lowest mitotic activity for any individual rat as the mean value of any sample, at any given time, was likely to vary significantly. In view of this fact, it was only possible, in any one graph composed of a series of observations on different animals, to locate a period characterised by a high rate of mitosis in consecutive samples and a period characterised by a low rate of mitosis in the consecutive samples. Any variation, in the course of such a period of high or low mitotic activity, by a single sample might possibly be due to individual variation. The grand mean of these/

Individual variation Group (Natural Lighting Conditions)

Table showing the individual variation in the average mitotic activity per Section (10μ) of the Oesophagus (epithelium) of 12 rats kept under natural lighting conditions of day and night and killed between 10.00 and 11.00 hours.

Rat No:	56	47	45	46	48	49	50	51	52	53	54	55
Mean No: of Mitoses per Section	8.3	15.4	12.0	9.4	8.0	15.8	6.8	14.6	38.8	34.5	27.1	6.3
S.D.	2.5	3.7	4.0	3.3	2.7	4.4	2.3	3.4	3.9	4.6	4.0	2.2
Variance	6.6	14.2	16.4	11.0	7.3	20.0	5.6	11.8	15.9	21.2	16.4	5.1
Range	2 to 15	8 to 23	2 to 24	1 to 16	3 to 13	7 to 13	2 to 11	9 to 23	29 to 49	24 to 49	16 to 34	2 to 10

Table No: 1

Average number of cells in the basal layer of the oesophageal epithelium of the adult rat.

Serial no: of Section	1	2	3	4	5	6	7	8
No: of Cells observed	1300	850	1075	1205	985	1044	1456	1313

Mean - 1153.

NO: 15

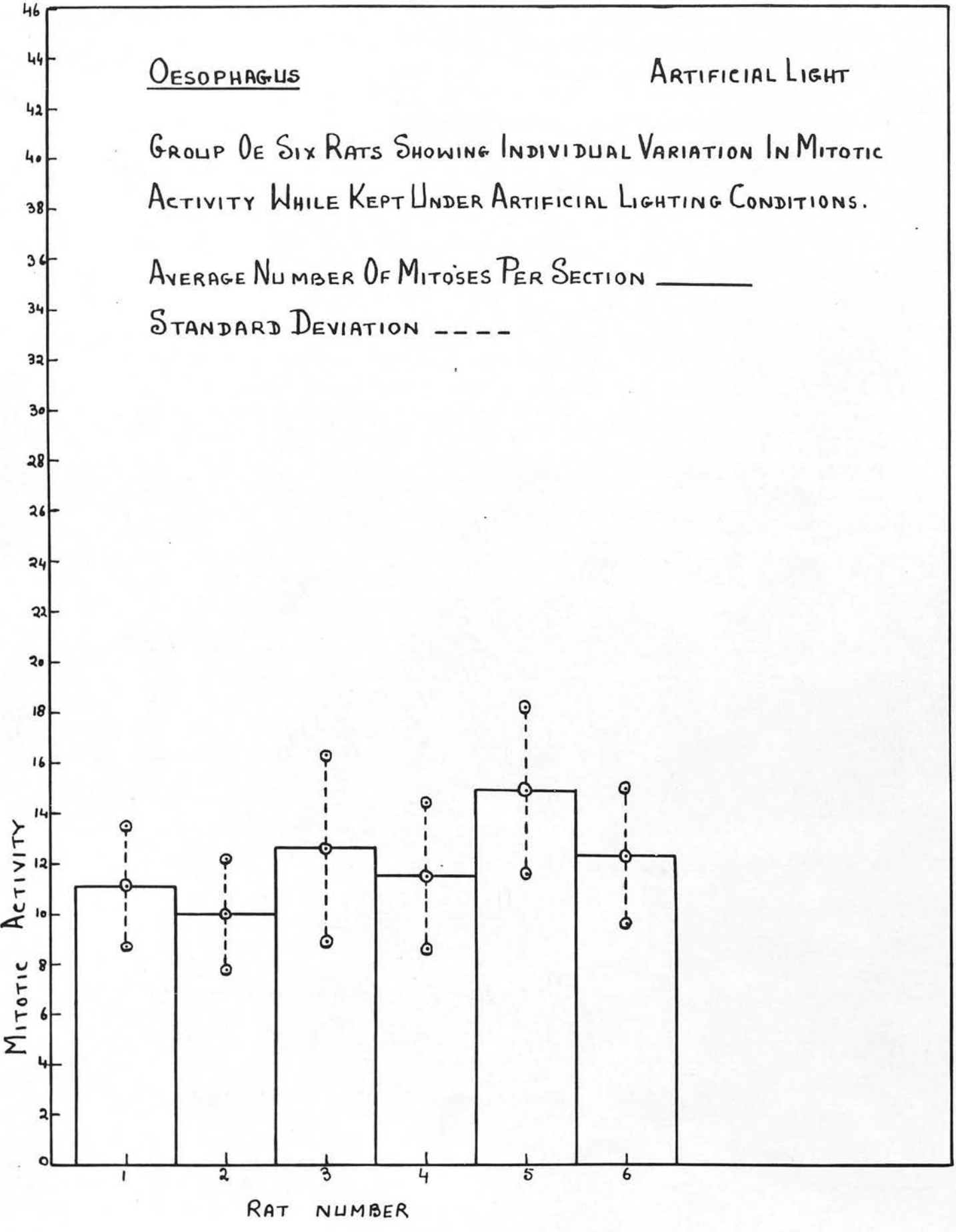
OESOPHAGUS

ARTIFICIAL LIGHT

GROUP OE SIX RATS SHOWING INDIVIDUAL VARIATION IN MITOTIC ACTIVITY WHILE KEPT UNDER ARTIFICIAL LIGHTING CONDITIONS.

AVERAGE NUMBER OF MITOSES PER SECTION _____

STANDARD DEVIATION - - - -



these 12 means had a very large standard deviation which also suggested a wide range of individual variation in the mitotic activity of different rats killed at the same time.

(Artificial Lighting Conditions)

A group of 6 rats, kept under artificial lighting conditions (light, 09.00 to 17.00 hours and darkness, 17.00 to 09.00 hours), were used to determine the range of individual variation in the mitotic activity; vide table no: 2 and graph no: 15.

All the 6 rats were killed at a time when a high rate of mitosis was expected. The average number of mitoses per section showed that the trend of the results was quite different from that obtained from the rats kept under natural lighting conditions. The mean values of the individual samples did not show any significant range of variation.

CONTROL GROUP Natural Lighting

(Skin Series)

A group of 12 rats was examined in this series. Having been kept under natural lighting conditions of day and night, one rat was killed every 2 hours during a 24-hour period. A sample of the skin of the ear was examined from each animal and the rate of mitosis expressed as the number

of/

Individual variation Group (Artificial lighting Conditions)

Table showing the individual variation in the average mitotic activity per Section (10μ) of the Oesophagus (epithelium) of 6 rats kept under artificial lighting conditions (light 09.00 to 17.00 hours and dark 17.00 to 09.00 hours) and killed between 12.00 and 13.00 hours.

Rat No:	69	70	71	72	73	74
Mean No; of Mitoses per Section	11.1	10.0	12.6	11.5	14.9	12.3
S.D.	2.4	2.2	3.7	2.9	3.3	2.7
Variance	5.8	5.2	13.7	8.9	10.9	7.4
Range	6 to 14	5 to 15	6 to 19	5 to 17	9 to 23	6 to 22

Table No: 2

NO: 1

SKIN

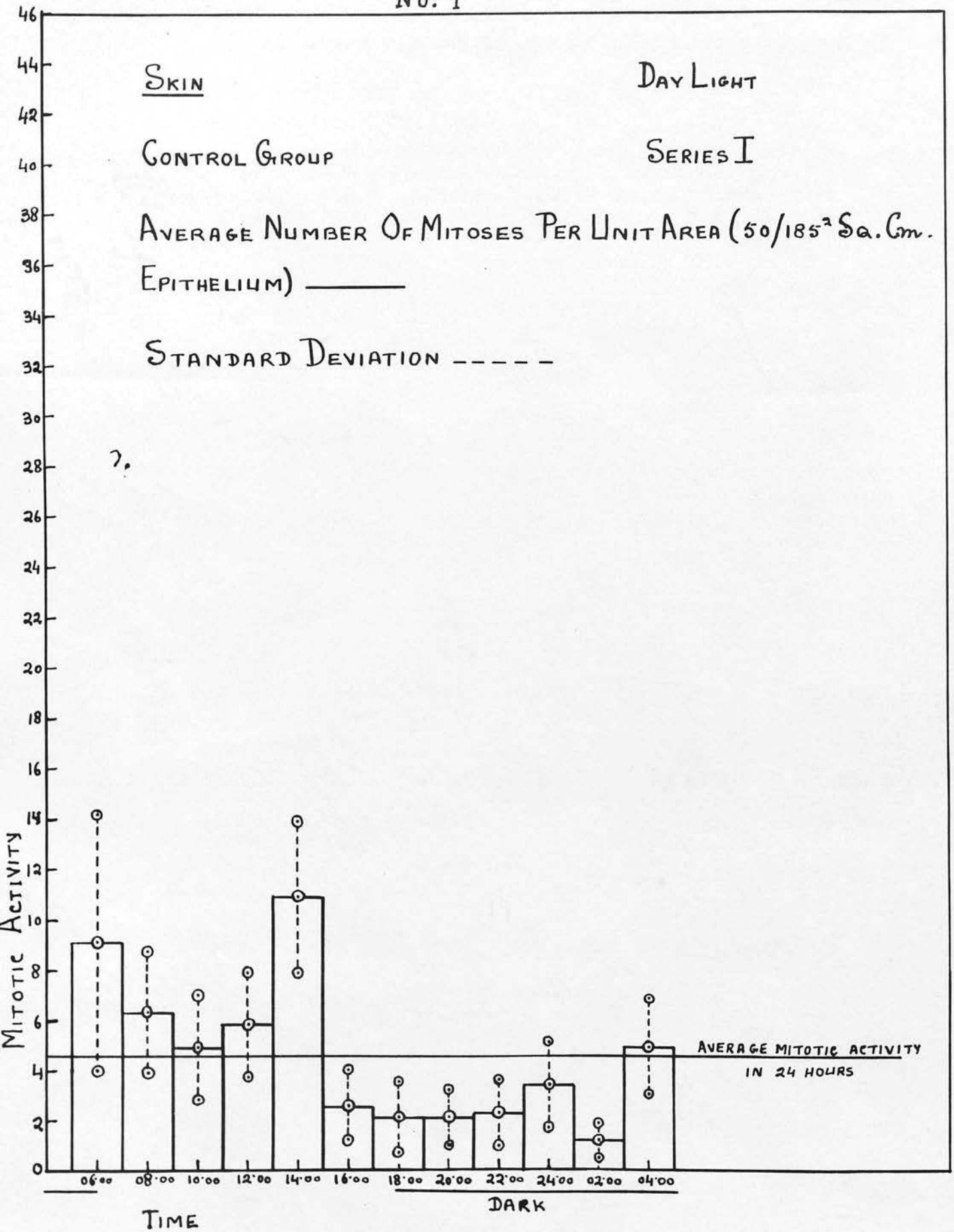
DAY LIGHT

CONTROL GROUP

SERIES I

AVERAGE NUMBER OF MITOSES PER UNIT AREA (50/185² Sq. Cm. EPITHELIUM) ——

STANDARD DEVIATION - - - - -



of mitoses per unit area ($50/185^2$ sq.cm.) of epithelium; vide table no: 3 and graph no: 1.

A definite periodicity in the mitotic activity was noticed in the course of a 24-hour period with maximum at 14.00 hours and minimum at 02.00 hours. The values for maximum and minimum mitotic activity were put to the test of significance and the value of 't' was found to be 21.6. In view of 89 "degrees of freedom" in this case, the 't' value indicated that the difference between maximum and minimum rates of mitosis was statistically significant. The average rate of mitosis during 24 hours was 4.6 mitoses per unit area. For the convenience of study, it was considered fairly reasonable to regard the mean values above this average figure as indicating a high rate of mitosis and the mean values below this average figure as indicating a low rate of mitosis. Thus, a period of high mitotic activity was noticed to occur from 04.00 to 14.00 hours and a period of low mitotic activity from 16.00 to 02.00 hours. Evidently, both the periods of high and low mitotic activity extended for a continuous period of approximately 12 hours.

The animals were exposed to day light for 12 hours (06.00 to 18.00 hours) and darkness 12 hours (18.00 to 06.00 hours), vide graph no: 1. In a general way, the lighting conditions bore a relationship to the mitotic activity, a high rate of mitosis occurring during the greater part of the day/

Control Group

Series I

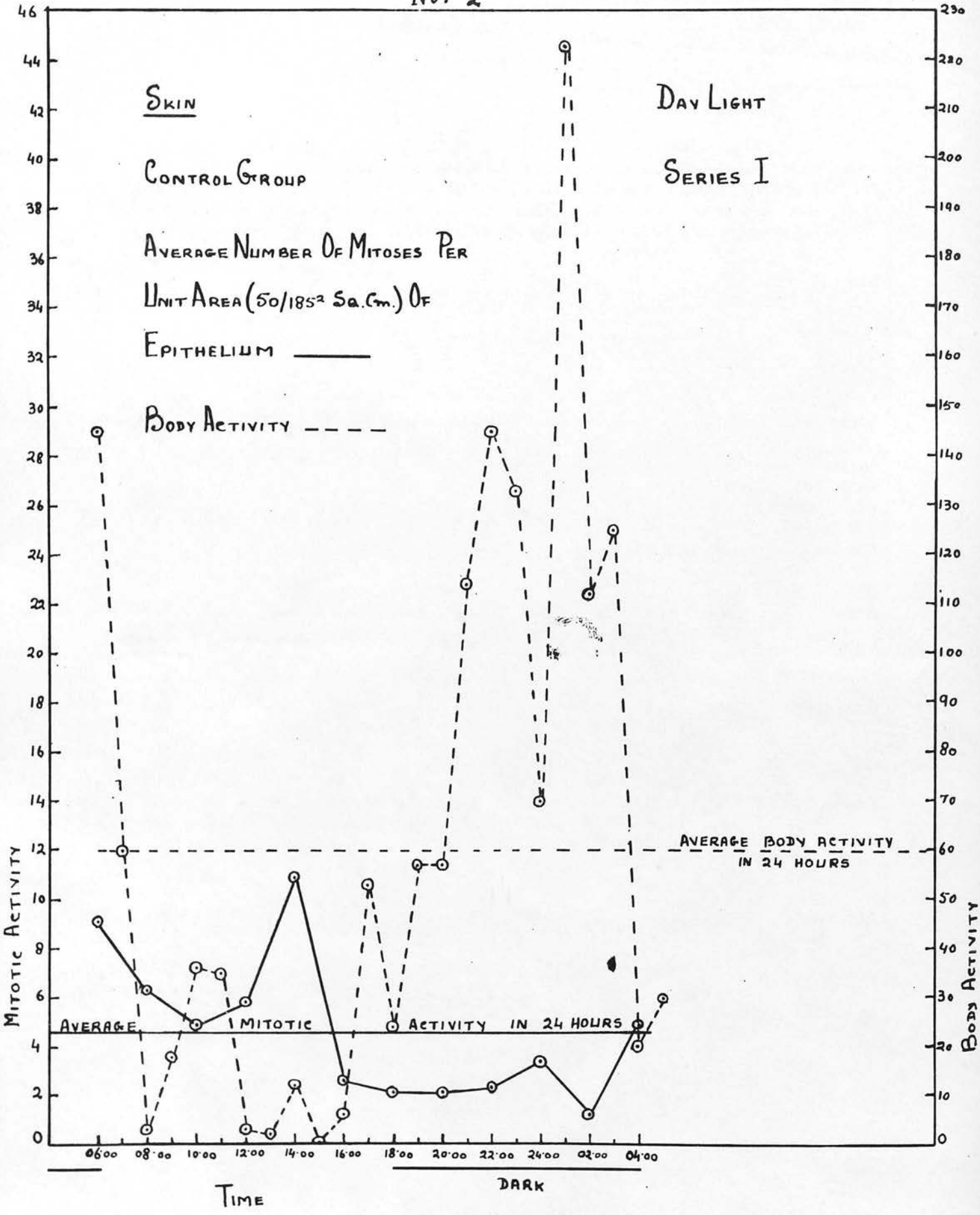
Skin

Table showing the average mitotic activity per unit area in the epithelium of ear skin of 12 male rats kept under natural lighting conditions of day and night (light 05.00 to 18.00 hours and dark 18.00 to 05.00 hours) and one being killed at 2 hourly intervals in the course of a 24 hour period.

Time	06.00	08.00	10.00	12.00	14.00	16.00	18.00	20.00	22.00	24.00	02.00	04.00
Mean No: of Mitoses per unit area	9.1	6.3	4.9	5.8	10.9	2.6	2.1	2.1	2.3	3.4	1.2	4.9
S.D.	5.1	2.4	2.1	2.1	3.0	1.4	1.4	1.1	1.3	1.7	0.7	1.9
Variance	26.9	6.1	4.7	4.6	9.4	2.1	2.0	1.4	1.7	2.9	0.6	3.8
Range	1.1 to 21.2	1.2 to 11.6	1.1 to 10.0	1.1 to 11.2	2.0 to 19.0	0.0 to 7.2	0.0 to 6.6	0.0 to 4.4	0.0 to 5.9	0.0 to 7.7	0.0 to 3.0	1.0 to 11.2
Rat No:	9	4	7	6	2	5	8	3	1	11	10	12

Table No: 3

NO: 2


SKIN
CONTROL GROUP
AVERAGE NUMBER OF MITOSES PER UNIT AREA (50/185² Sq.Cm.) OF EPITHELIUM ——
BODY ACTIVITY - - - -
DAY LIGHT
SERIES I
AVERAGE BODY ACTIVITY IN 24 HOURS
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
BODY ACTIVITY
TIME
DARK
06·00
08·00
10·00
12·00
14·00
16·00
18·00
20·00
22·00
24·00
02·00
04·00

day and a low rate of mitosis during the greater part of the night. It was, however, noticed that, in the afternoon, the mitotic activity fell to a low value 3 hours before the onset of darkness and remained low until the 9th hour of the dark period. The mitotic activity rose again 3 hours before the onset of light and remained high until the 9th hour of the light period. Moreover, it was found that the rise in the rate of mitosis occurred 9 hours after the onset of darkness and remained high for a period of 12 hours.

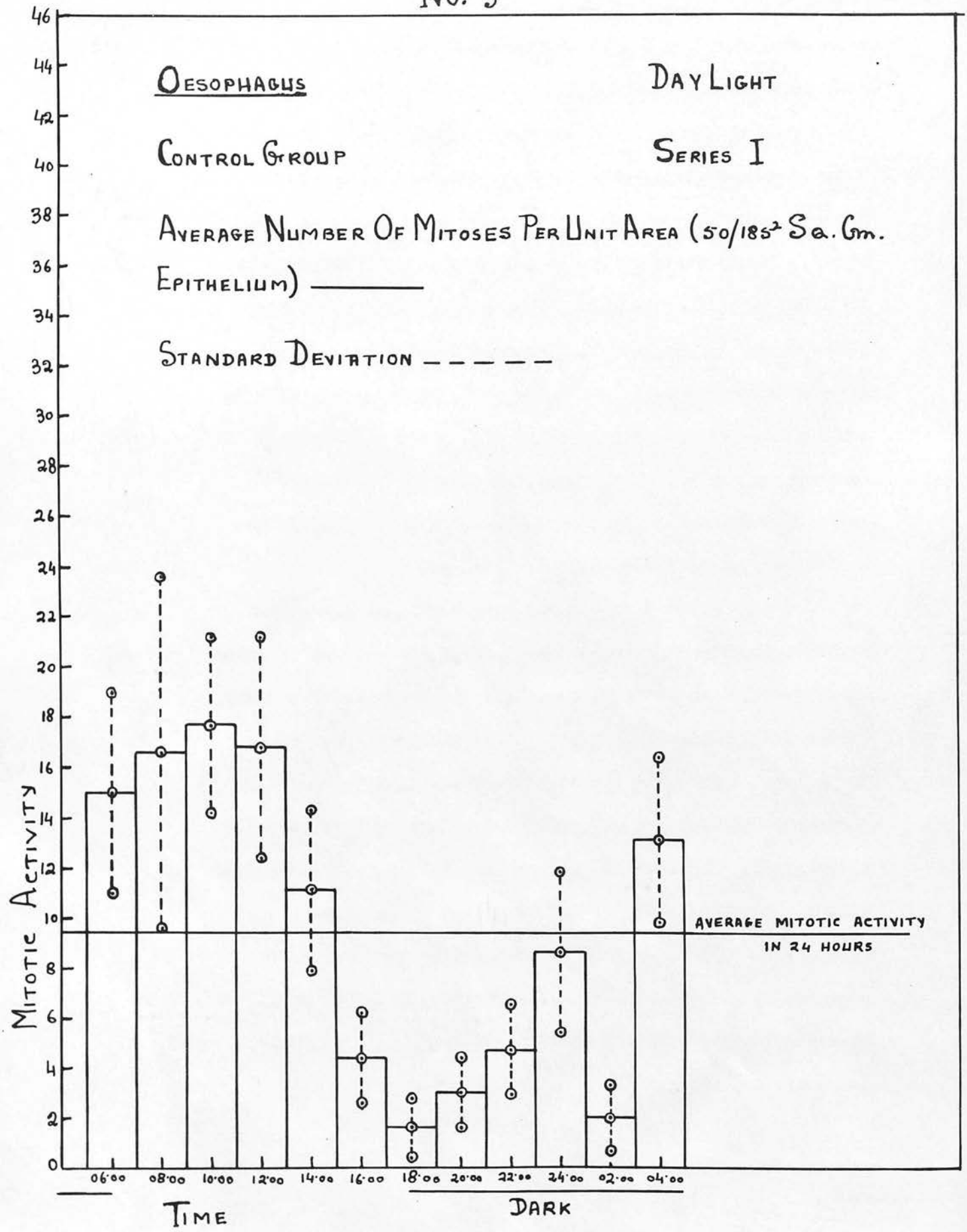
The relationship between mitotic activity and body activity was a general one, vide graph no: 2. The curve representing the body activity was not smooth. It presented several fluctuations in the hourly observations which did not bear any relationship to the corresponding observations of the mitotic activity. The average body activity in 24 hours was 60 per hour. For the convenience of study, it was considered reasonable to regard the values above this average figure as indicating a high body activity and the values below this average figure as indicating a low body activity. It was thus found that the body activity curve exhibited two periods of high and two of low body activity. The primary period of low body activity extended for 13 hours and was followed by the primary period of high body activity for 7 hours. Afterwards, a secondary 2-hour interval of low body activity occurred, followed by a secondary 2-hour interval of high/

high body activity. When the curves of mitotic activity and body activity were compared, it was noticed that, broadly, the period of high mitotic activity coincided with the primary period of low body activity and the period of low mitotic activity with the primary period of high body activity. It was further noticed that the mitotic activity fell to a low value 6 hours before the primary rise in the body activity and it remained low throughout the primary period of high body activity. Towards the early morning, the rise in the mitotic activity was associated with the primary fall in the body activity. From this time onwards the mitotic activity remained high for a period of 12 hours despite the secondary rise in the body activity at 06.00 hours.

With regard to the relationship between the body activity and the lighting conditions, it was noticed that the onset of darkness was followed, after an interval of 3 hours, by the primary rise in the body activity which remained high for 7 hours though the period of darkness continued for another 3 hours. The entire secondary interval of low body activity and the first half of the secondary interval of high body activity occurred during the period of darkness. The onset of the morning light was followed, after an interval of 2 hours, by the secondary fall in the body activity which remained low throughout the period of light and the first 3 hours of darkness.

CONTROL GROUP/

NO: 3


OESOPHAGUS
DAY LIGHT
CONTROL GROUP
SERIES I
AVERAGE NUMBER OF MITOSES PER UNIT AREA (50/185² Sq. Gm. EPITHELIUM) ——
STANDARD DEVIATION – – – – –
MITOTIC ACTIVITY
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
46
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
06·00
08·00
10·00
12·00
14·00
16·00
18·00
20·00
22·00
24·00
02·00
04·00
TIME
DARK

CONTROL GROUP
Oesophagus

(Series I) (Natural Lighting)

The rate of mitosis in the squamous epithelium of the oesophagus was studied from the same set of 12 rats as that used for the skin. The oesophagus was removed from each rat for examination, one having been killed every 2 hours during a period of 24 hours. The mitotic activity was expressed in two ways, (1) Average number of mitoses per unit area ($50/185^2$ sq.cm.) of epithelium and (2) Average number of mitoses per section (10 μ) of the oesophagus.

(1) A distinct periodicity in the mitotic activity was found to occur in the course of 24 hours with the maximum rate of mitosis at 10.00 hours and the minimum at 18.00 hours; vide table no: 4 and graph no: 3. The values for maximum and minimum mitotic activity were put to the test of significance and the 't' value was found to be 30.9. In view of 98 "degrees of freedom" in this case, the 't' value showed that the difference between the maximum and minimum mitotic activity was statistically significant. The average mitotic activity during 24 hours was 9.5 mitoses per unit area. Thus, a period of high mitotic activity was seen to occur from 04.00 to 14.00 hours and a period of low mitotic activity from 16.00 to 02.00 hours, that is, both the periods of high and low mitotic activity extended for 12 hours. Towards the end of the period of low mitotic activity, there was a suggestion of a small rise in the rate of mitosis./

Control Group

Series I

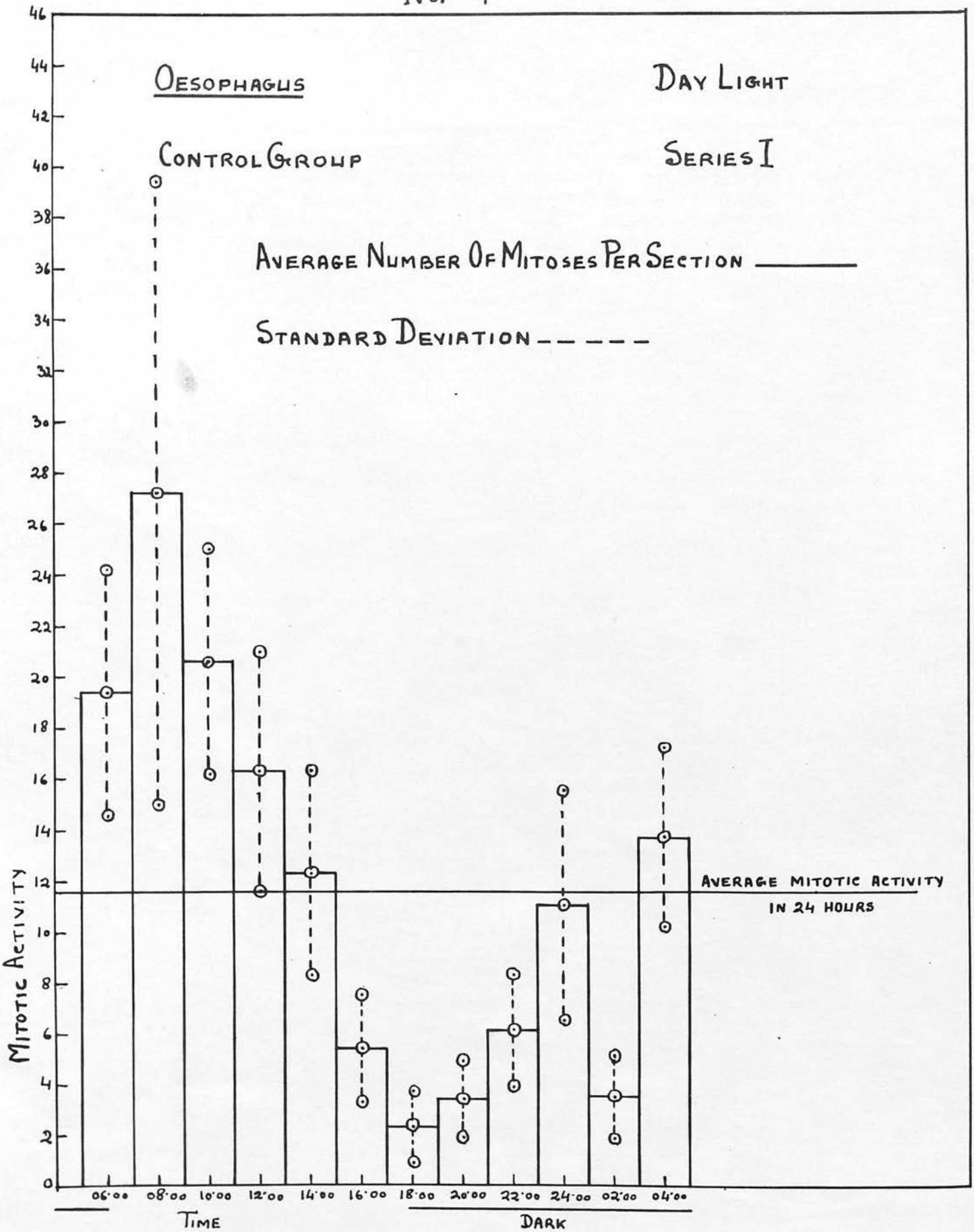
Oesophagus

Table showing the average mitotic activity per unit area in the Squamous epithelium of the Oesophagus of 12 male rats kept under natural lighting conditions of day and night (light 05.00 to 18.00 hours and dark 18.00 to 05.00 hours) and one being killed at 2 hourly intervals in the course of a 24 hour period.

Time	06.00	08.00	10.00	12.00	14.00	16.00	18.00	20.00	22.00	24.00	02.00	04.00
Mean No: of Mitoses per unit area	15.0	16.6	17.7	16.8	11.1	4.4	1.6	3.0	4.7	8.6	2.0	13.1
S.D.	4.0	7.0	3.5	4.4	3.2	1.8	1.2	1.4	1.8	3.2	1.3	3.3
Variance	16.1	50.0	12.4	20.2	10.3	3.6	1.5	2.1	3.3	10.5	1.8	10.9
Range	7.1 to 24.5	5.2 to 32.5	12.6 to 29.1	5.5 to 26.9	5.2 to 18.0	1.0 to 9.0	0.0 to 5.5	0.0 to 6.6	0.9 to 7.9	3.0 to 19.1	0.0 to 7.1	7.1 to 20.0
Rat No:	9	4	7	6	2	5	8	3	1	11	10	12

Table No: 4

NO: 4


OESOPHAGUS
DAY LIGHT
CONTROL GROUP
SERIES I
AVERAGE NUMBER OF MITOSES PER SECTION
STANDARD DEVIATION
MITOTIC ACTIVITY
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
46
06·00
08·00
10·00
12·00
14·00
16·00
18·00
20·00
22·00
24·00
02·00
04·00
TIME
DARK

mitosis.

(2) No significant difference in the result occurred when the mitotic activity was expressed as the number of mitoses per section; vide table no: 5 and graph no: 4. The only difference observed was that, on the whole, the mean values of all the samples were now slightly increased and the peak, at 10.00 hours in the former case, had now shifted to 08.00 hours. The overall rise in all the mean values was accounted for by the fact that the area of the epithelium per section in most of the samples was greater than the unit area used in the former case. The shift of the peak was accounted for by the fact that the area of the epithelium in the sample at 08.00 hours was comparatively greater than that in the sample at 10.00 hours. So, in the course of adjustment of the number of mitoses to the unit area ($50/185^2$ sq.cm.) of epithelium, the number of mitoses in the sample at 08.00 hours was reduced proportionately more than the number of mitoses in the sample at 10.00 hours.

As in the case of the skin, exposure to day light extended for 12 hours (06.00 to 18.00 hours) and darkness for 12 hours (18.00 to 06.00 hours); vide graph nos: 3 and 4. The lighting conditions bore a general relationship to the mitotic activity, a high rate of mitosis occurring during the greater part of the day and a low rate of mitosis during the greater part of the night. It was further noticed that, in the/

Control Group — Series I

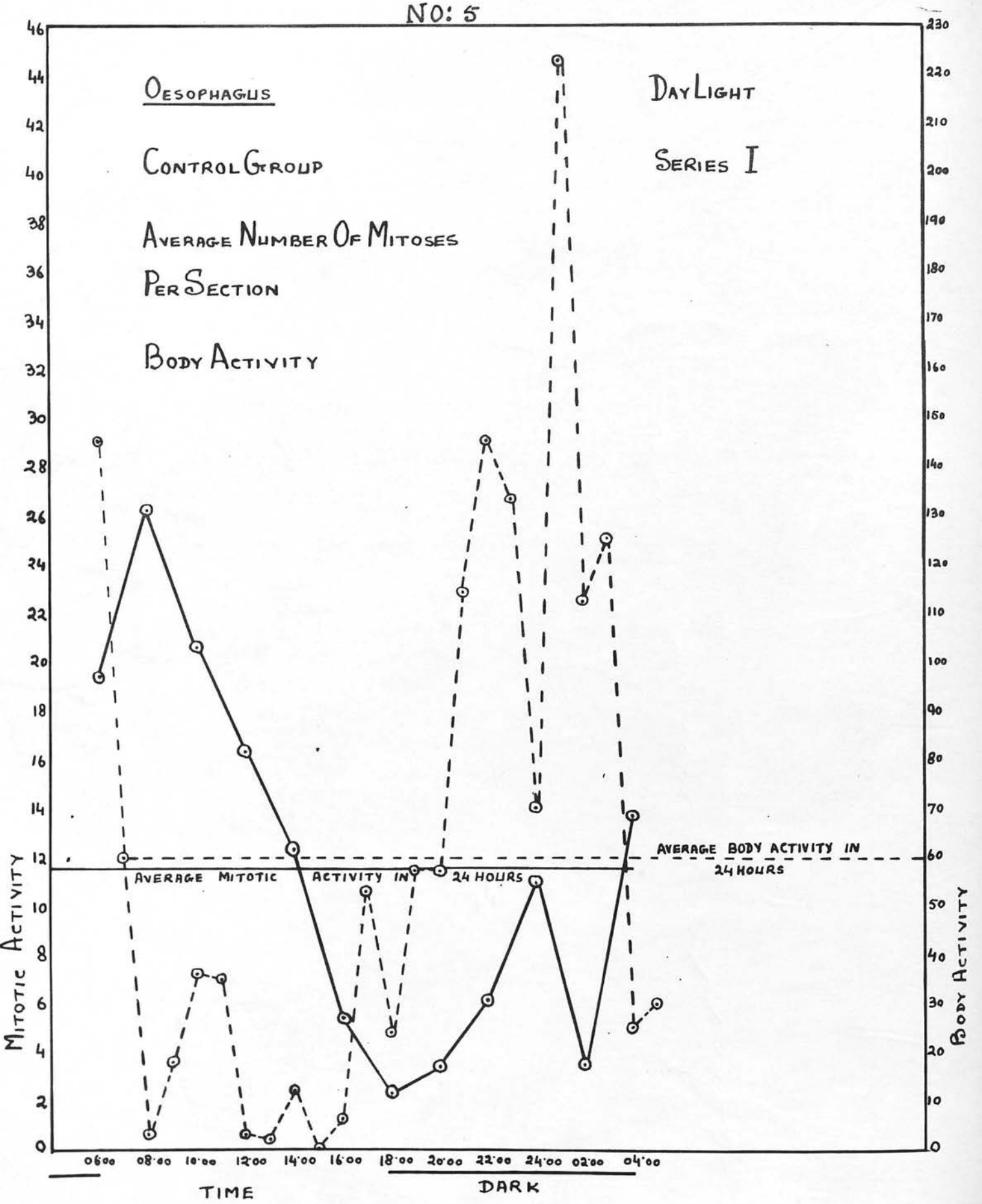
Oesophagus

Table showing the average mitotic activity per Section (10μ) in the Squamous epithelium of the Oesophagus of 12 male rats kept under natural lighting conditions of day and night (light 05.00 to 18.00 hours and dark 18.00 to 05.00 hours) and one being killed at 2 hourly intervals in the course of a 24 hour period.

Time	06.00	08.00	10.00	12.00	14.00	16.00	18.00	20.00	22.00	24.00	02.00	04.00
Mean No: of Mitoses per Section	19.4	27.2	20.6	16.3	12.3	5.4	2.3	3.4	6.1	11.0	3.5	13.7
S.D.	4.8	12.2	4.4	4.7	4.0	2.1	1.4	1.5	2.2	4.5	1.6	3.5
Variance	23.9	155.8	20.0	22.3	16.0	4.5	2.0	2.3	4.9	20.8	2.6	12.3
Range	10 to 30	9 to 62	11 to 35	5 to 30	5 to 20	1 to 10	0 to 5	0 to 6	1 to 10	3 to 23	0 to 7	6 to 21
Rat No:	9	4	7	6	2	5	8	3	1	11	10	12

Table No: 5

NO: 5


OESOPHAGUS
CONTROL GROUP
AVERAGE NUMBER OF MITOSES PER SECTION
BODY ACTIVITY
DAYLIGHT
SERIES I
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
AVERAGE BODY ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
BODY ACTIVITY
0600 0800 1000 1200 1400 1600 1800 2000 2200 2400 0200 0400
TIME
DARK

the afternoon, the mitotic activity fell to a low value 3 hours before the onset of darkness and remained low until the 9th hour of the dark period except for a suggestion of a small rise in the rate of mitosis at 24.00 hours. The mitotic activity rose again 3 hours before the onset of light and remained high until the 9th hour of the light period. In addition, it was found that the rise in the rate of mitosis occurred 9 hours after the onset of darkness and remained high for 12 hours.

The curve representing the body activity was not smooth; vide graph no: 5. It presented several fluctuations in the hourly observations which did not bear any relation to the corresponding observations of the mitotic activity. The average body activity during 24 hours was 60 per hour and the body activity curve exhibited two periods of high and two of low body activity. The primary period of low body activity extended for 13 hours and was followed by the primary period of high body activity for 7 hours. Soon after, a secondary 2-hour interval of low body activity was noticed to occur, followed by a secondary 2-hour interval of high body activity. Comparison of the curves of mitotic activity and body activity showed that, broadly, the period of high mitotic activity coincided with the primary period of low body activity and the period of low mitotic activity with the primary period of high body activity. At the same time, it was noticed that the mitotic/

mitotic activity fell to a low value 6 hours before the primary rise in the body activity and remained low throughout the primary period of high body activity. Towards the early morning, the rise in the mitotic activity was closely associated with the primary fall in the body activity, both preceding the onset of daylight. From this time onwards the mitotic activity remained high until 14.00 hours despite the secondary rise in the body activity at 06.00 hours.

With regard to the relationship of the body activity to the lighting conditions, it was observed that the onset of darkness was followed, after an interval of 3 hours, by the primary rise in the body activity which remained high for 7 hours though the period of darkness continued for another 3 hours. The entire secondary interval of low body activity and the first half of the secondary interval of high body activity occurred while it was still dark. The onset of the morning light at 06.00 hours was followed, after an interval of 2 hours, by the secondary fall in the body activity which remained low throughout the period of light and the first 3 hours of darkness.

On the completion of the investigation of the mitotic activity in the skin and the oesophagus of Series I, it was decided to abandon further investigations on the skin and to continue work on oesophagus only and to determine the mitotic/

mitotic activity in the epithelium of this organ as the number of mitoses per section. This decision was taken for the following reasons:-

(1) Various authors, in the past, had carried out extensive work on the mitotic activity in the skin of the mouse with special reference to diurnal variation.

(2) The technique, employed in the present work for investigating the mitotic activity in the skin, required a considerable amount of time and was less accurate owing to the presence of hairs and the difficulty which arose as a result of excluding the follicles from the adjacent skin. As a result of this, a fairly long period was required to collect sufficient observations in order to produce reliable figures for the mitotic activity in the skin.

(3) As it was proposed to study the effects of light on the mitotic activity in tissues in general, the oesophagus was thought to be a more suitable organ for this purpose as it was not directly exposed to the light.

(4) With regard to the oesophagus, the method employed for expressing the mitotic activity as the number of mitoses per unit area of epithelium ensured accurate results but was a time-consuming one. On the other hand, the method used for expressing the mitotic activity as the number of mitoses per section, though less accurate, was more rapid. Admittedly, the quick method produced results which were not so/

so accurate or so strictly comparable, due to the unequal area of epithelium in different sections of the same oesophagus and in the oesophagus of different animals. But this fact brought only a small error into the results, as was evident from the fact that the results of Series I, expressed by the two methods mentioned above, were almost similar. In view of the above considerations, it was decided to sacrifice some accuracy of the technique as it was considered that this would not materially affect the results.

CONTROL GROUP
Oesophagus

(Series II) (Natural Lighting)

The 12 rats of this series had been kept under natural lighting conditions in which day light extended for 17 hours (04.00 to 21.00 hours) and darkness for 7 hours (21.00 to 04.00 hours). This change in the duration of light and darkness, as compared to Series I, was due to the fact that the two series of experiments were carried out at different times of the year. One rat was killed every 2 hours during a period of 24 hours and the mitotic activity was expressed as the number of mitoses per section; vide table no: 6 and graph no: 6.

The mitotic activity curve showed the standard periodicity during a 24-hour period, with the maximum at 10.00 hours/

Control Group

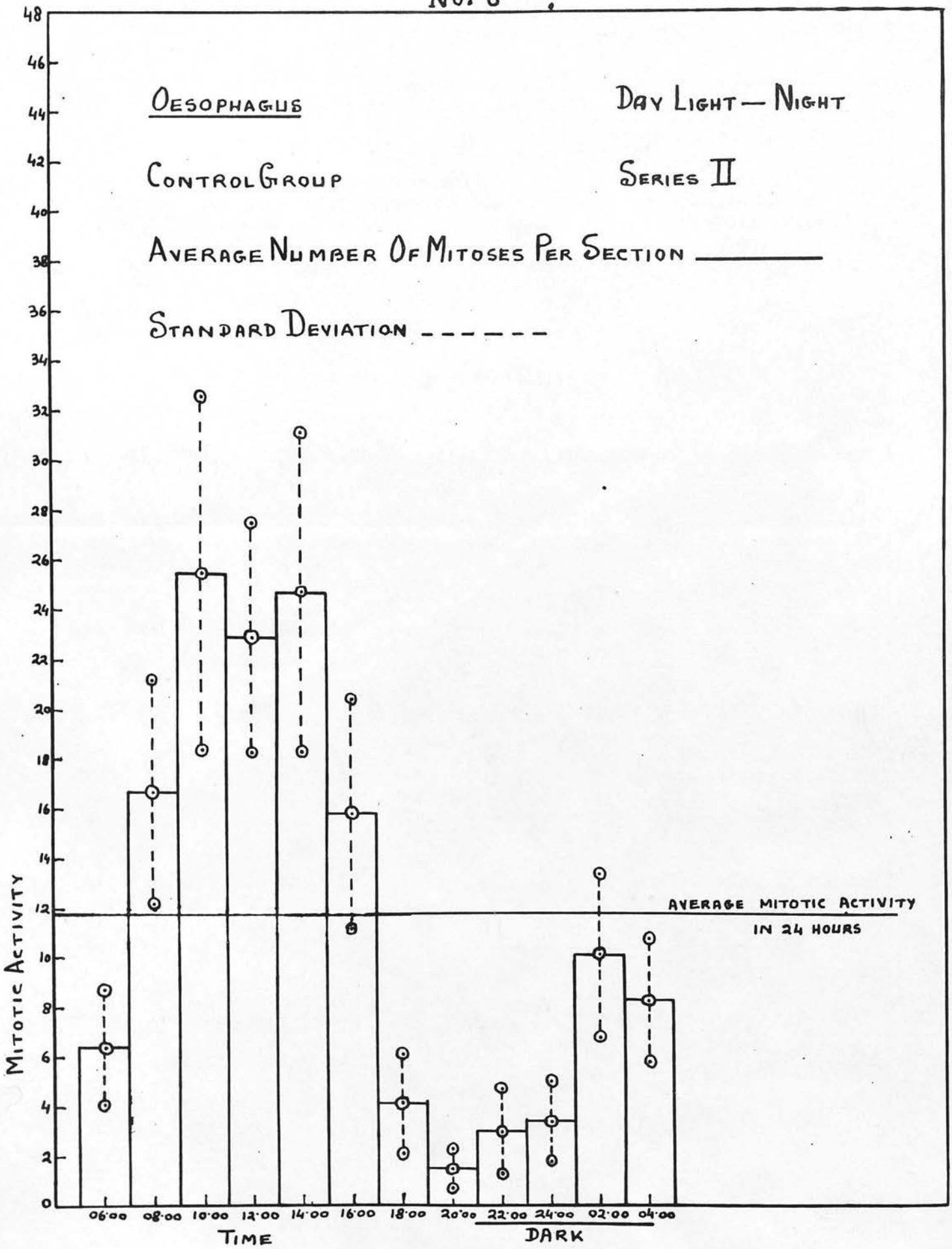
Series II

Table showing the average mitotic activity per Section (10^{M}) in the Squamous epithelium of the Oesophagus of 12 male rats kept under natural lighting conditions of day and night (Light 04.00 to 21.00 hours and dark 21.00 to 04.00 hours) and one being killed at 2 hourly intervals in the course of a 24 hour period.

Time	06.00	08.00	10.00	12.00	14.00	16.00	18.00	20.00	22.00	24.00	02.00	04.00
Mean No: of Mitoses per Section	6.4	16.7	25.5	22.9	24.7	15.8	4.1	1.5	3.0	3.4	10.1	8.3
S.D.	2.3	3.6	4.5	4.0	6.6	3.3	2.0	0.8	1.7	1.6	3.5	3.2
Variance	5.5	13.2	21.1	16.3	44.8	11.5	4.3	0.7	2.9	2.6	12.6	10.4
Range	1 to 11	6 to 23	8 to 26	7 to 24	5 to 32	2 to 18	0 to 9	0 to 3	0 to 7	0 to 7	6 to 18	4 to 19
Rat No:	20	13	17	21	15	22	23	24	25	26	18	19

Table No: 6

NO: 6

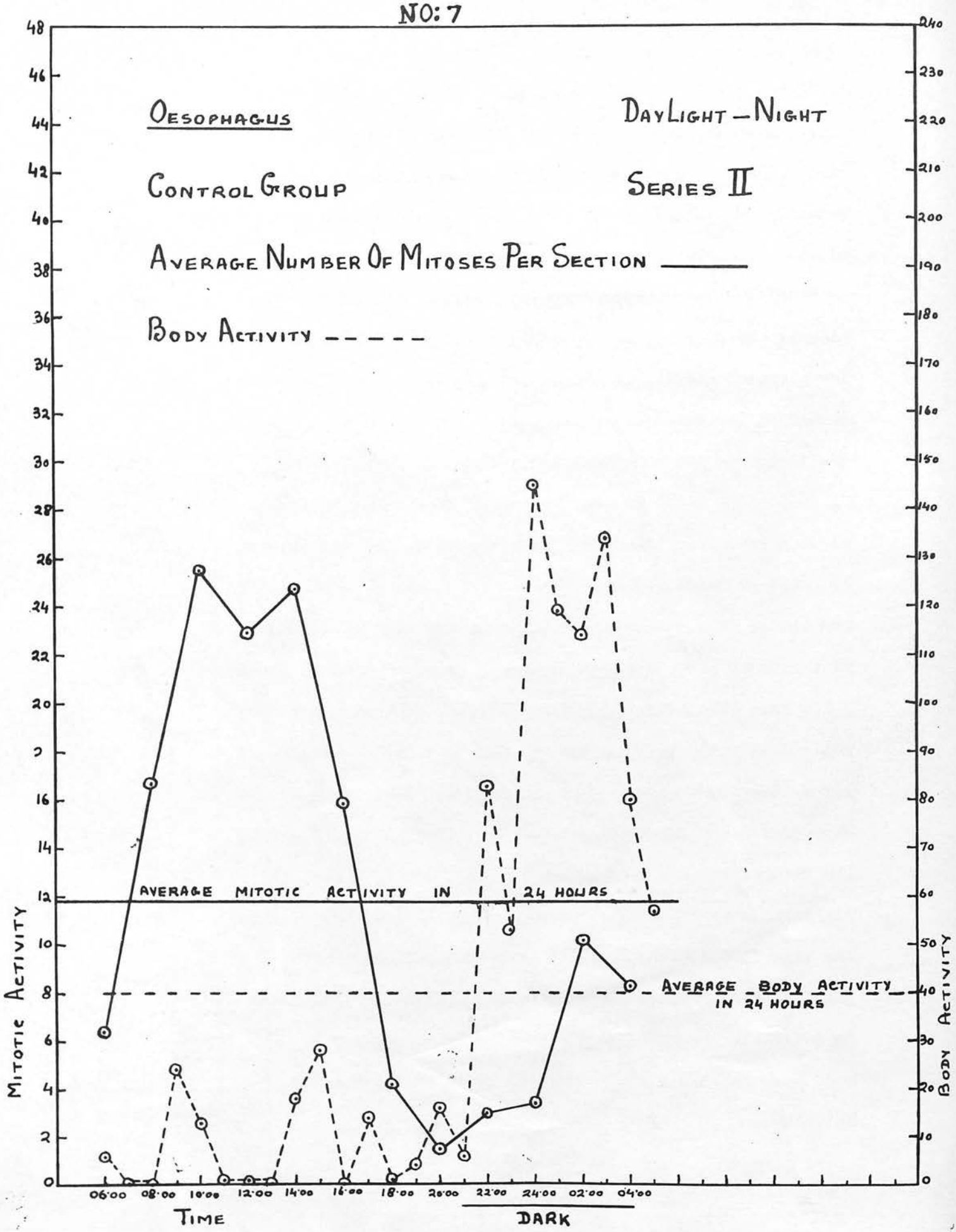

OESOPHAGUS
DAY LIGHT — NIGHT
CONTROL GROUP
SERIES II
AVERAGE NUMBER OF MITOSES PER SECTION
STANDARD DEVIATION
MITOTIC ACTIVITY
AVERAGE MITOTIC ACTIVITY
IN 24 HOURS
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
46
48
06·00
08·00
10·00
12·00
14·00
16·00
18·00
20·00
22·00
24·00
02·00
04·00
TIME
DARK

10.00 hours and the minimum at 20.00 hours. The 't' value (33.1) with the corresponding 88 "degrees of freedom" showed that the difference between the maximum and minimum mitotic activity was statistically significant. Since the average mitotic activity throughout 24 hours was 11.9 mitoses per section, a period of high mitotic activity (more than 11.9 mitoses per section) extended for 10 hours and a period of low mitotic activity for 14 hours. Towards the end of the period of low mitotic activity, there was a suggestion of a small rise in the rate of mitosis at 02.00 hours.

The lighting conditions, to which reference has already been made, were such that day light was present for 17 hours and darkness for 7 hours. Here again the lighting conditions bore a general relation to the mitotic activity, a high rate of mitosis occurring during the period of light and a low rate of mitosis during the night. It was further noticed that the rate of mitosis fell to a low value 4 hours before the onset of darkness and remained low throughout the dark period and for 3 hours after the onset of light. Thus the rate of mitosis rose again 3 hours after the onset of light and remained so for a period of 10 hours. In addition, the rise in the mitotic activity occurred 10 hours after the onset of darkness, an interval almost similar to that found in Series I.

In this series also, the relation between the mitotic/

NO: 7

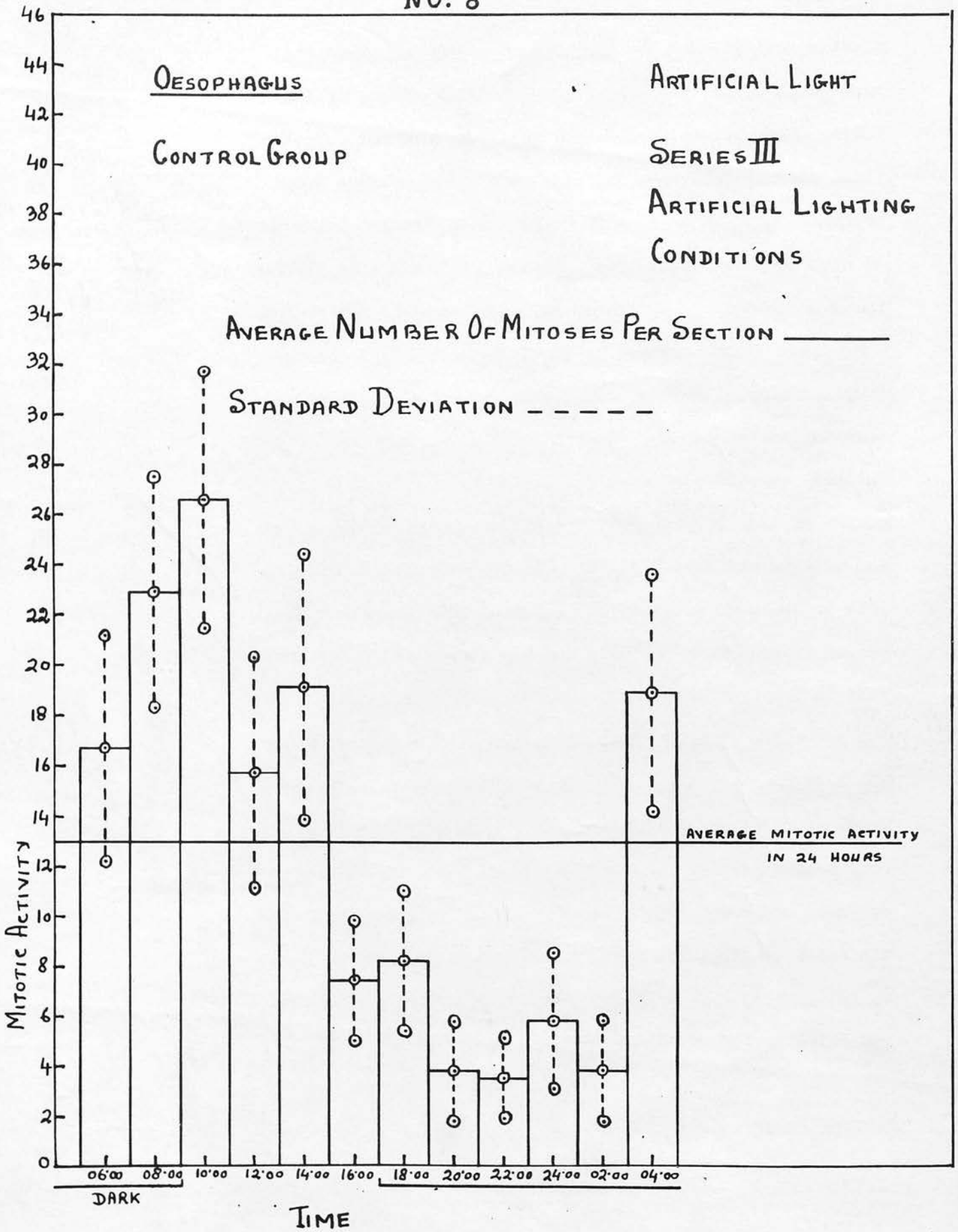

OESOPHAGUS
DAYLIGHT – NIGHT
CONTROL GROUP
SERIES II
AVERAGE NUMBER OF MITOSES PER SECTION
BODY ACTIVITY
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
AVERAGE BODY ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
BODY ACTIVITY
06·00 08·00 10·00 12·00 14·00 16·00 18·00 20·00 22·00 24·00 02·00 04·00
TIME
DARK

mitotic activity and the body activity was a general one; vide graph no: 7. Although several fluctuations in the hourly observations of the body activity were noticed, a distinct diurnal variation was observed. The average body activity in the course of 24 hours was 40 per hour, the period of high body activity, when this value was exceeded, lasted for 8 hours and the period of low body activity for 16 hours. Comparison of the curves, of the mitotic activity and the body activity, revealed that the period of high mitotic activity coincided approximately with the period of low body activity and the period of low mitotic activity with the period of high body activity. It was clear, however, that the mitotic activity fell to a low value 5 hours before the rise in the body activity and remained low throughout the period of high body activity and the first hour after the fall in the body activity.

The standard feature in the relationship between the body activity and the lighting conditions was that the onset of darkness was immediately followed by a rise in the body activity which remained high throughout the period of darkness and for 1 hour after the onset of light. As such, the onset of light was followed, after an interval of 2 hours, by the fall in body activity which remained low during the remaining period of illumination.

CONTROL GROUP/

NO: 8


OESOPHAGUS
CONTROL GROUP
ARTIFICIAL LIGHT
SERIES III
ARTIFICIAL LIGHTING CONDITIONS
AVERAGE NUMBER OF MITOSES PER SECTION
STANDARD DEVIATION
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
46
06·00
08·00
10·00
12·00
14·00
16·00
18·00
20·00
22·00
24·00
02·00
04·00
DARK
TIME

CONTROL GROUP
Oesophagus

(Series III) (Artificial Lighting)

This series of 12 rats was kept under artificial lighting conditions for a period of 90 days, the duration of light being 8 hours (09.00 to 17.00 hours) and darkness 16 hours (17.00 to 09.00 hours), at the end of which one rat was killed every 2 hours during a 24-hour period. Mitotic activity in the epithelium of the oesophagus was expressed as the number of mitoses per section; vide table no: 7 and graph no: 8.

As in Series I and II, the mitotic curve showed the standard periodicity in the course of 24 hours. The maximum rate of mitosis occurred at 10.00 hours and the minimum at 22.00 hours. The 't' value (30.3) with the corresponding 98 "degrees of freedom" showed that the difference between the maximum and minimum mitotic activity was statistically significant. The average mitotic activity in 24 hours was 13 mitoses per section and it was noticed that both the periods of high and low mitotic activity occurred for 12 hours each.

The relationship of the mitotic activity to the lighting conditions was different from that observed in Series I and II. In a general way, a high rate of mitosis occurred during the greater part of the light period and a low rate of mitosis during the greater of the dark period. Detailed

study/

Control Group

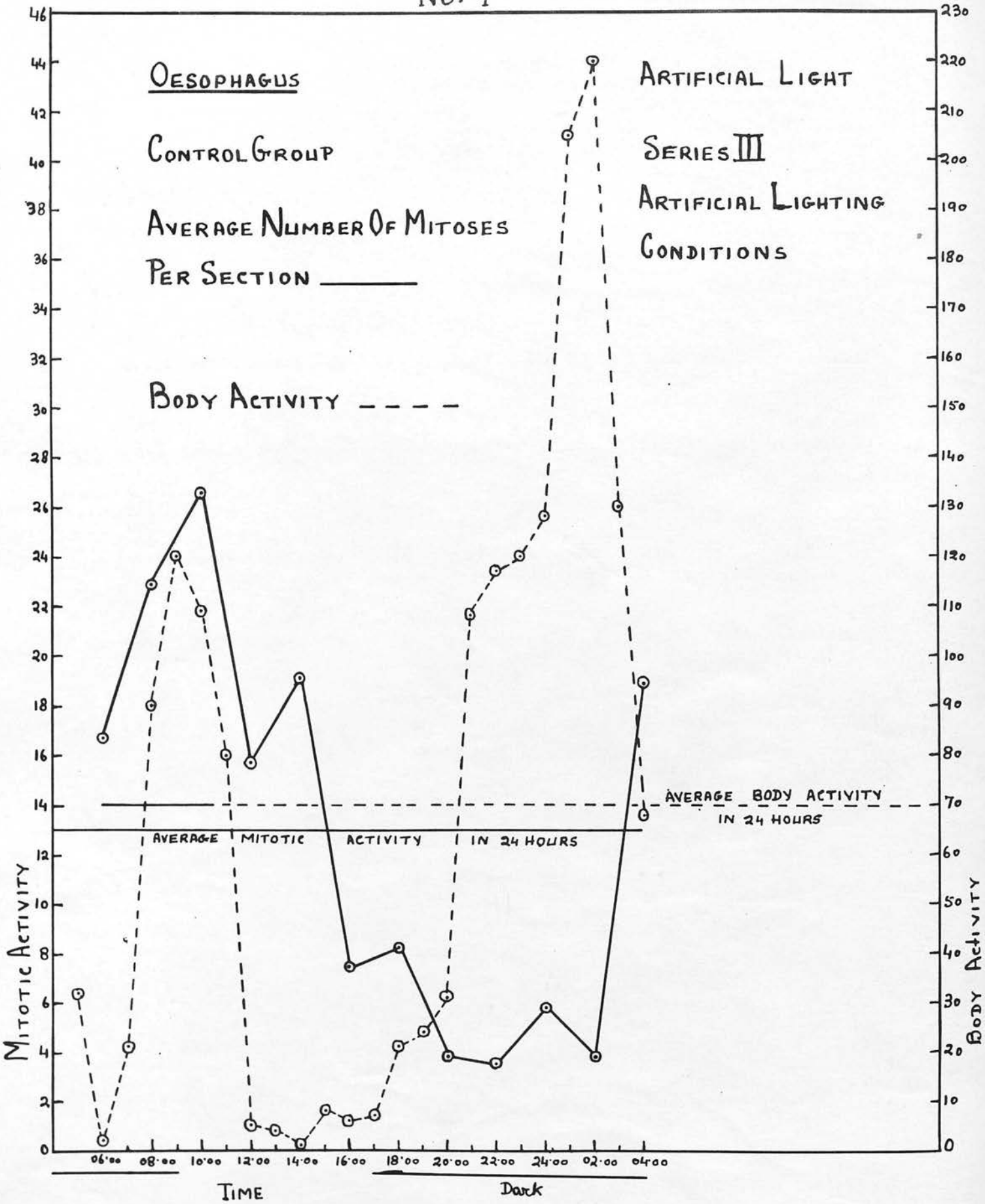
Series III

Table showing the average mitotic activity per Section (10µ) in the Squamous epithelium of the Oesophagus of 12 male rats kept under artificial lighting conditions (light 09.00 - 17.00 hours and dark 17.00 - 09.00 hours) and one being killed at 2 hourly intervals in the course of a 24 hour period.

Time	06.00	08.00	10.00	12.00	14.00	16.00	18.00	20.00	22.00	24.00	02.00	04.00
Mean No: of mitoses per Section	16.7	22.9	26.6	15.7	19.1	7.4	8.2	3.8	3.5	5.8	3.8	18.9
S.D.	4.5	4.6	5.1	4.6	5.3	2.4	2.8	2.0	1.6	2.7	2.0	4.7
Variance	20.5	21.5	27.0	21.4	28.6	6.1	8.4	4.2	2.8	7.8	4.3	22.1
Range	10-31	13-33	17-40	7-29	9-35	2-13	2-17	1-8	0-7	1-15	0-10	10-35
Rat No:	67	68	57	58	59	60	61	62	63	64	65	66

Table No: 7

NO: 9


OESOPHAGUS
CONTROL GROUP
AVERAGE NUMBER OF MITOSES PER SECTION
BODY ACTIVITY
ARTIFICIAL LIGHT
SERIES III
ARTIFICIAL LIGHTING CONDITIONS
AVERAGE BODY ACTIVITY IN 24 HOURS
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
BODY ACTIVITY
06·00 08·00 10·00 12·00 14·00 16·00 18·00 20·00 22·00 24·00 02·00 04·00
TIME
Dark

study showed that the mitotic activity fell to a low level 2 hours before the onset of darkness and remained low until the 10th hour of the dark period. The rate of mitosis rose again 6 hours before the onset of light and continued to be high until the 6th hour of the light period. In this case, the general relationship was distorted to such an extent that the first half of the period of high mitotic activity corresponded to the last 6 hours of darkness and the 2nd half of the period of high mitotic activity corresponded to the first 6 hours of the light period. However, the rise in the mitotic activity occurred 10 hours after the onset of darkness, this interval being similar to that found in Series II and only slightly different from that in Series I.

The curve representing the body activity (graph no: 9) was like that observed in Series I (graph no: 5). The average body activity in 24 hours was 70 per hour. The body activity curve presented two distinct periods of high body activity alternating with two periods of low body activity. The primary period of low body activity extended for 9 hours and was followed by the primary period of high body activity for 7 hours. Then, a secondary 4-hour interval of low body activity occurred, followed by a secondary 4-hour interval of high body activity. On comparing the curve of the mitotic activity with that of the body activity, it was found that the mitotic activity fell to a low value 6 hours before the

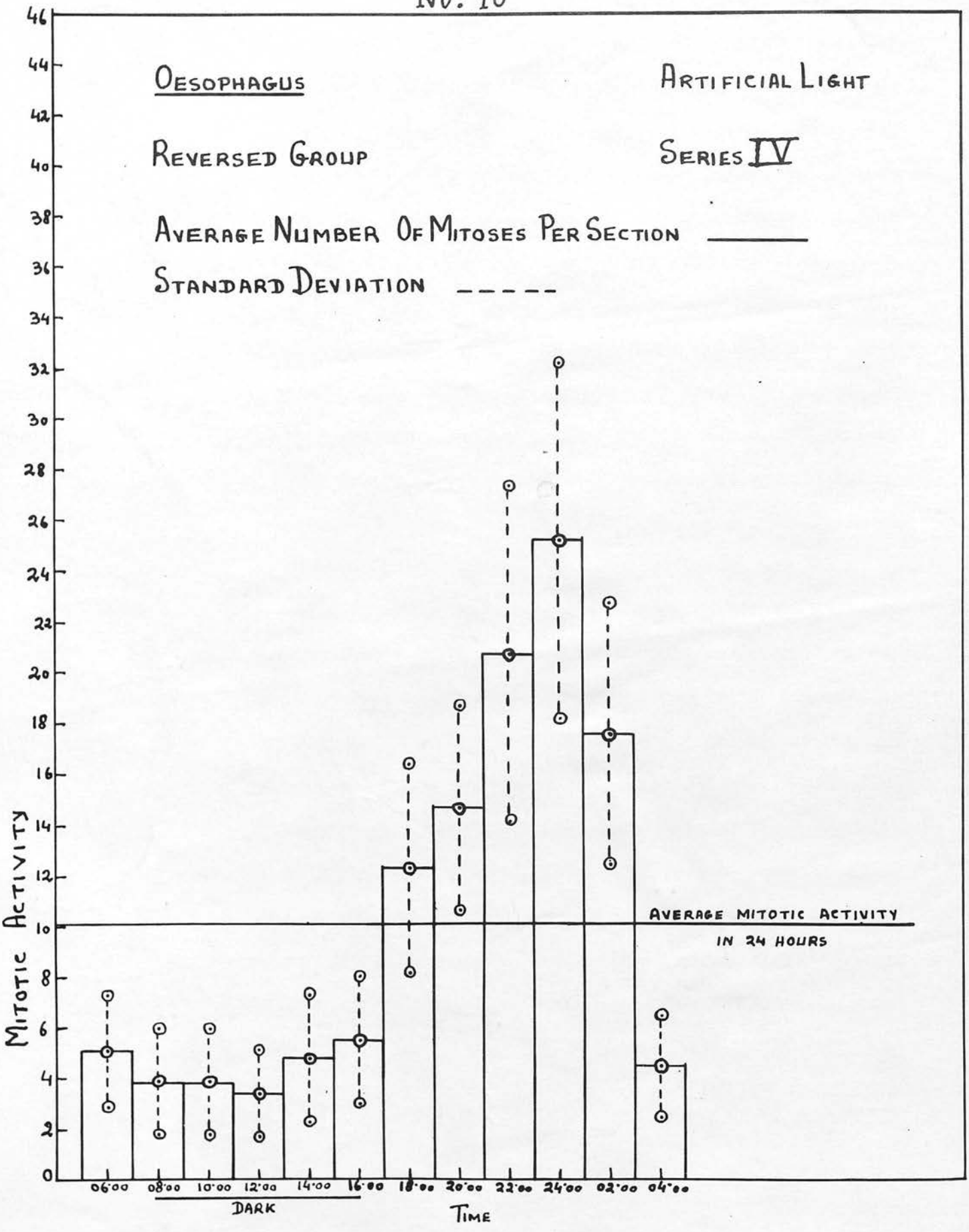
primary/

primary rise in the body activity and remained low throughout the primary period of high body activity. The subsequent rise in the mitotic activity, as in Series I and II, was closely associated with the primary fall in the body activity and it remained high for a period of 12 hours despite the secondary 4-hour interval of high body activity. The overall relation of the mitotic activity to the body activity, in this case, resembled the conditions noticed in Series I but was completely different from that found in Series II. So much so that the period of high mitotic activity coincided with a period of high body activity, a feature also present in Series I but not so pronounced.

The relationship between the body activity and the lighting conditions showed that the onset of darkness was followed, after an interval of 4 hours, by the primary rise in the body activity which remained high for a period of only 7 hours though darkness continued for another 6 hours. As in Series I, the entire secondary interval of low body activity and first half of the secondary interval of high body activity occurred while it was still dark. The onset of light was followed, after an interval of 3 hours, by the secondary fall in the body activity which remained low throughout the period of light and the first 3 hours of darkness.

REVERSED GROUP
Oesophagus /

NO: 10


OESOPHAGUS
ARTIFICIAL LIGHT
REVERSED GROUP
SERIES IV
AVERAGE NUMBER OF MITOSES PER SECTION
STANDARD DEVIATION
MITOTIC ACTIVITY
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
46
AVERAGE MITOTIC ACTIVITY
IN 24 HOURS
06·00
08·00
10·00
12·00
14·00
16·00
18·00
20·00
22·00
24·00
02·00
04·00
DARK
TIME

REVERSED GROUP
Oesophagus

(Series IV) (Artificial Lighting)

The 12 rats of this series were kept under reversed conditions of artificial lighting for a period of 90 days, the period of light being 16 hours (16.00 to 08.00 hours) and darkness 8 hours (08.00 to 16.00 hours). At the end of this period, the rats were killed, one every 2 hours throughout a 24-hour period. As in the other series, the mitotic activity was studied and expressed as the number of mitoses per section; vide table no: 8 and graph no: 10.

Just as in the case of Series I,II and III, the mitotic activity curve exhibited a standard periodicity during a 24-hour period. But, in this series, the mitotic activity curve was noticed to have completely reversed with the reversal in the lighting conditions. As a result of this, it was seen that now the period of high mitotic activity occurred during the period of low mitotic activity in the control group and the period of low mitotic activity during the period of high mitotic activity in the control group. The maximum rate of mitosis occurred at 24.00 hours and the minimum at 12.00 hours. From the test of significance, the 't' value (21.3) corresponding to 98 "degrees of freedom" indicated that the difference between the maximum and minimum rates of mitosis was statistically significant. The average mitotic/

Reversed Group

Series IV

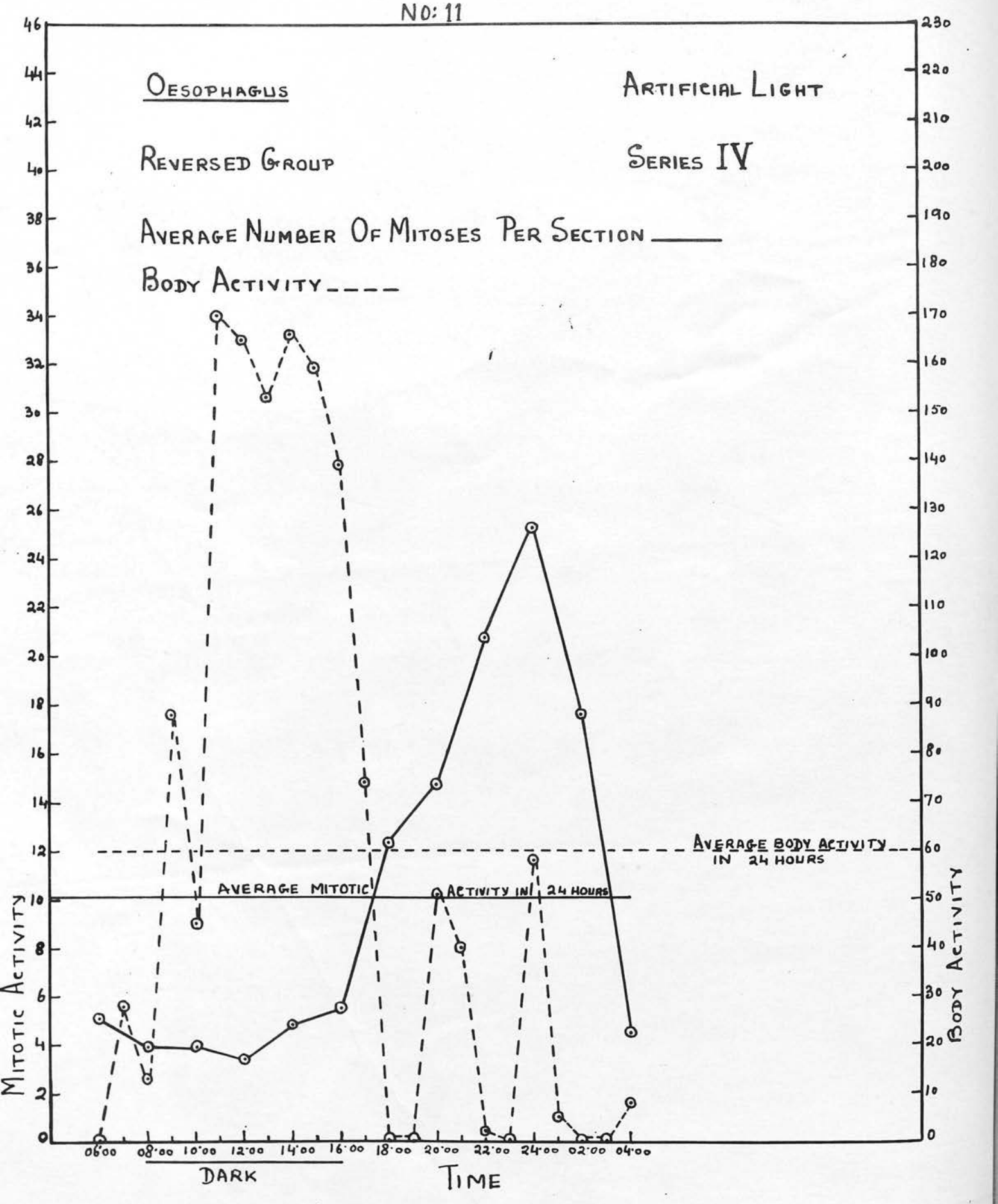
Oesophagus

Table showing the average number of mitoses per Section (10M) in the Squamous epithelium of the Oesophagus of 12 male rats kept under reversed artificial lighting conditions (light 16.00 to 08.00 hours and dark 08.00 to 16.00 hours) and one being killed at 2 hourly intervals in the course of a 24 hour period.

Time	06.00	08.00	10.00	12.00	14.00	16.00	18.00	20.00	22.00	24.00	02.00	04.00
Mean No: of Mitoses per Section	5.1	3.9	3.9	3.4	4.8	5.5	12.3	14.7	20.7	25.2	17.6	4.5
S.D.	2.2	2.0	2.1	1.7	2.5	2.5	4.1	4.0	6.6	7.0	5.1	2.0
Variance	5.1	4.0	4.7	3.0	6.6	6.6	17.3	16.1	44.1	49.3	26.2	4.0
Range	1 to 9	0 to 9	0 to 11	0 to 8	0 to 10	1 to 13	5 to 22	6 to 27	7 to 36	10 to 44	7 to 28	0 to 9
Rat No:	40	42	27	28	29	30	32	33	35	36	37	39

Table No: 8

NO: 11


OESOPHAGUS
ARTIFICIAL LIGHT
REVERSED GROUP
SERIES IV
AVERAGE NUMBER OF MITOSES PER SECTION
BODY ACTIVITY
AVERAGE BODY ACTIVITY IN 24 HOURS
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
BODY ACTIVITY
06·00
08·00
10·00
12·00
14·00
16·00
18·00
20·00
22·00
24·00
02·00
04·00
DARK
TIME

mitotic activity in the course of 24 hours was 10.1 mitoses per section and a period of high mitotic activity (more than 10.1 mitoses per section) occurred for 10 hours and a period of low mitotic activity for 14 hours.

The lighting conditions, to which reference has already been made, were such that illumination was continued for 16 hours and darkness for 8 hours. The lighting conditions bore a general relation to the mitotic activity, a high rate of mitosis occurring during the period of light and a low rate of mitosis during the period of darkness. At the end of the period of high mitotic activity, the rate of mitosis fell to a low level 5 hours before the onset of darkness and remained low throughout the dark period and the first hour after the onset of light. Naturally then, the rate of mitosis rose again 1 hour after the onset of light and remained so for a period of 10 hours. In addition, it was noticed that the interval between the onset of darkness and the rise in the mitotic activity was 9 hours, a period very similar to that observed in Series I, II and III.

As a result of the reversal in the lighting conditions, the periodicity in the body activity was also reversed and its general inverse relationship to the mitotic activity maintained as in the previous series of experiments; vide graph no: 11. The average body activity in a 24-hour period was 60 per hour. The period of high body activity extended for 9 hours, except for a small drop at 10.00 hours, and the period of low body activity for/

for 15 hours. Comparison of the curves of the mitotic activity and the body activity showed that the rate of mitosis fell to a low value 6 hours before the rise in the body activity and continued to be low throughout the period of high body activity. At the end of the period of low mitotic activity, it was noticed that the rise in the rate of mitosis and the fall in the body activity occurred almost simultaneously.

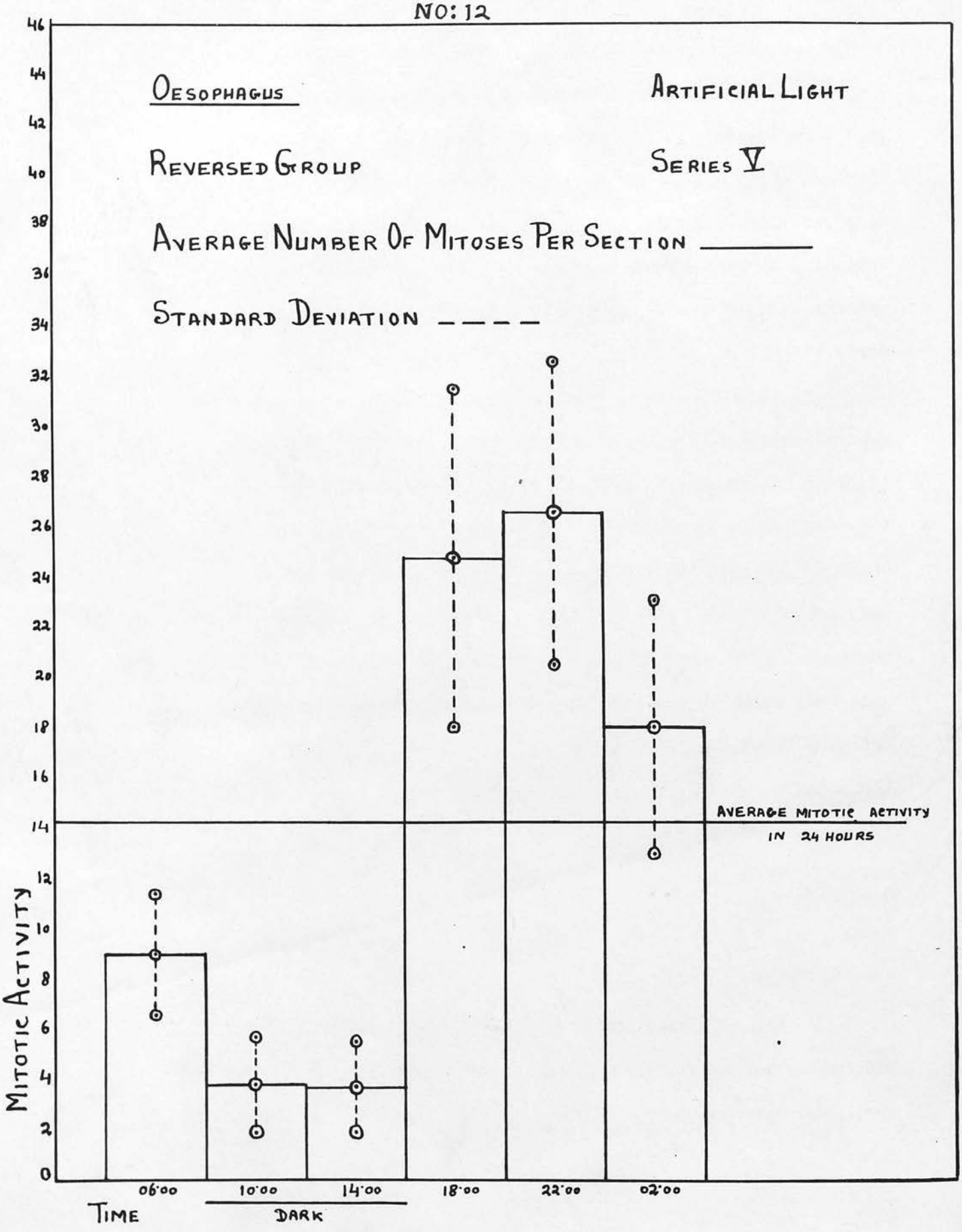
Although the lighting conditions were reversed, the general relationship of the body activity with the periods of light and darkness continued to exist as noticed in the previous series of experiments. It was further noticed that the onset of darkness was immediately followed by a rise in the body activity which remained high throughout the period of darkness. The onset of light, on the other hand, was followed, after an interval of 2 hours, by a fall in the body activity which remained low throughout the period of light (16 hours).

REVERSED GROUP
Oesophagus

(Series V) (Artificial Lighting)

Six rats examined in this series were kept under reversed conditions of artificial lighting for a period of 90 days, the duration of light being 16 hours (16.00 to 08.00 hours)/

NO: 12


OESOPHAGUS
ARTIFICIAL LIGHT
REVERSED GROUP
SERIES V
AVERAGE NUMBER OF MITOSES PER SECTION
STANDARD DEVIATION
AVERAGE MITOTIC ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
46
06·00
10·00
14·00
18·00
22·00
02·00
TIME
DARK

hours) and that of darkness 8 hours (08.00 to 16.00 hours). The rats were killed, one every 4 hours during a 24-hour period. The mitotic activity, in the epithelium of the oesophagus, was determined as the number of mitoses per section; vide table no: 9 and graph no: 12.

The number of observations in the course of 24 hours, though less than in Series IV, showed the characteristic periodicity of mitotic activity. Exactly as in Series IV, the mitotic activity curve was noticed to have completely reversed with the reversal in the lighting conditions. It was seen that the period of high mitotic activity occurred during the period of low mitotic activity in the control group and the period of low mitotic activity during the period of high mitotic activity of the control group. The maximum rate of mitosis was seen to occur at 22.00 hours and the minimum at 14.00 hours. In view of the 't' value (25.9) and the corresponding 98 "degrees of freedom", the difference between the maximum and minimum rates of mitosis was significant. The average rate of mitosis in the course of 24 hours was 14.3 mitoses per section and the periods of high and low mitotic activity were of 12 hours each.

As already mentioned, the animals in this series were exposed to light for 16 hours out of the 24 hours in each day; vide graph no: 12. Here also, the lighting conditions bore a general relationship to the mitotic activity, a high

rate/

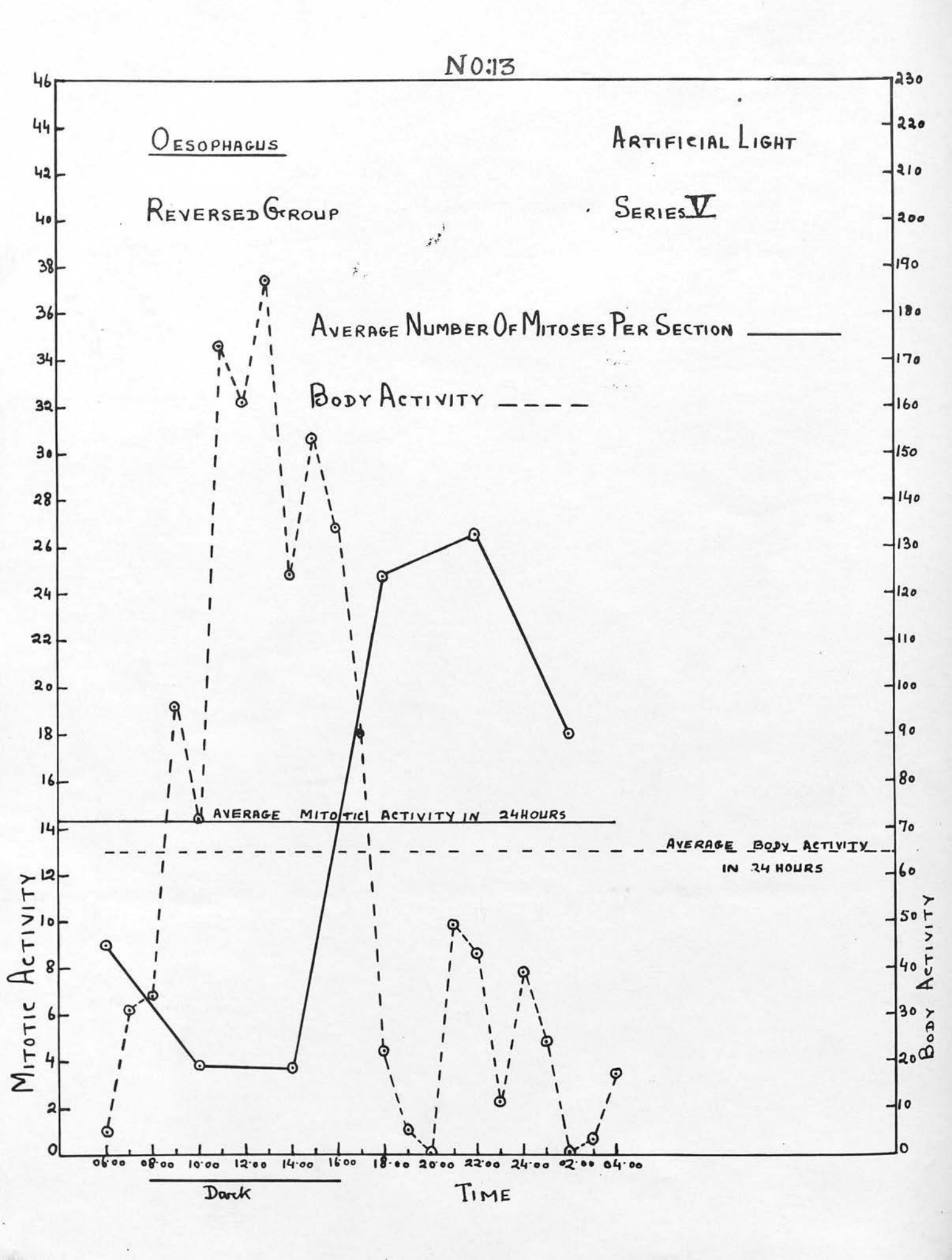
Reversed Group

Series V

Table showing the average mitotic activity per Section (10μ) in the Squamous epithelium of the Oesophagus of 6 rats (male) kept under reversed artificial lighting conditions (light 16.00 to 08.00 hours and dark 08.00 to 16.00 hours) and one being killed at 4 hourly intervals in the course of 24 hours.

Time	06.00	10.00	14.00	18.00	22.00	02.00
Mean No: of Mitoses per Section	9.0	3.8	3.7	24.7	26.5	18.0
S.D.	2.4	1.9	1.8	6.7	6.0	5.0
Variance	6.1	3.9	3.4	45.8	36.6	25.5
Range	1 to 14	0 to 8	0 to 7	10 to 39	14 to 39	9 to 33
Rat No:	41	43	44	31	34	38

Table No: 9


NO:13
OESOPHAGUS
ARTIFICIAL LIGHT
REVERSED GROUP
SERIES V
AVERAGE NUMBER OF MITOSES PER SECTION
BODY ACTIVITY
AVERAGE MITOTIC ACTIVITY IN 24HOURS
AVERAGE BODY ACTIVITY IN 24 HOURS
MITOTIC ACTIVITY
BODY ACTIVITY
TIME
Dark
06·00 08·00 10·00 12·00 14·00 16·00 18·00 20·00 22·00 24·00 02·00 04·00

rate of mitosis being present during the period of light and a low rate of mitosis during the period of darkness. It was further noticed that, at the end of the period of high mitotic activity, the rate of mitosis fell to a low value, approximately 4 hours before the onset of darkness, and it continued to be so throughout the period of darkness. The rate of mitosis rose again after the onset of light and remained high until the 12th hour of the light period. The interval between the onset of darkness and the rise in the mitotic activity, in this case, was 8 hours, a period similar to that observed in all the previous series of experiments but less satisfactory as a measurement in view of the smaller number of animals.

In this series as well, the periodicity in the body activity was reversed with the reversal in the lighting conditions and the general inverse relationship between the mitotic activity and the body activity continued to be maintained; vide graph no: 13. The average body activity in 24 hours was 65 per hour and the period of high body activity lasted for 9 hours and the period of low body activity for 15 hours. Comparison of the curves of the mitotic activity and the body activity showed that the mitotic activity fell to a low value approximately 5 hours before the rise in the body activity and remained low approximately throughout the period of high body activity. At the end of the period of low mitotic activity,/

activity, the rise in the rate of mitosis and the fall in the body activity occurred almost simultaneously.

The general relationship between the body activity and the lighting conditions continued to exist, as in other series of experiments, even though the lighting conditions were reversed; vide graph no: 13. It was further noticed that the onset of darkness was soon followed by the rise in the body activity which lasted throughout the period of darkness. The onset of light, in this case, was followed, after an interval of 2 hours, by the fall in the body activity which remained low throughout the period of illumination (16 hours).

SUMMARY

(Control Group)

In all the three series of experiments, a distinct single diurnal cycle of mitotic activity occurred in the oesophageal epithelium. The duration of high mitotic activity varied from 10 to 12 hours and that of low mitotic activity from 12 to 14 hours. The duration of high mitotic activity in Series I and III was 12 hours, where the duration of darkness was longer than in Series II. Though, in a general way, high mitotic activity was associated with light and low mitotic activity with darkness, the periods of high

and/

and low mitotic activity were not restricted to the respective periods of light and darkness. It was thus noticed that when the duration of darkness was short, 7 hours in Series II, the entire 10-hour interval of high mitotic activity occurred during the light period. With an increase in the duration of darkness, 12 hours in Series I, the first 3 hours of high mitotic activity occurred during the last 3 hours of the dark period. When the duration of darkness was 16 hours in Series III, the first half of the 12-hour period of high mitotic activity fell during the last 6 hours of the period of darkness. Another noticeable feature was that the rise in the mitotic activity followed the onset of darkness after an interval (9 to 10 hours) which was very similar in all the three series of experiments; vide graph no: 19. The similarity of these intervals combined with the varying length of the period of darkness led to more or less of the phase of high mitotic activity falling within the dark period. In addition, it was obvious from a comparison of the results in the first 3 series of experiments that the rise in the mitotic rate was not directly related to the onset of illumination; vide graph no: 20.

With regard to the body activity, it was found that there was a marked diurnal variation in the activity of the rat, high body activity tending to occur during the period of darkness and low body activity during the light. In addition, it/

it was noticed that, with short duration of darkness as in Series II, the animals, having rested throughout the long period of light, went in to activity soon after the onset of darkness and continued to be active for a period of 8 hours. In the case of longer periods of darkness, as in Series I and III, the animals, although nocturnal in habit, did not remain active throughout the period of darkness. They came to a resting phase after an interval of 7 hours which was very similar to that observed in Series II. But as darkness still continued, the rats, having rested a while, went into the secondary period of activity which lasted for 2 hours in Series I and 4 hours in Series III. After the two periods of high body activity in the case of the long period of darkness, as in Series I and III, the animals were faced with a short interval of light which was probably not enough for their rest. As a result of this, the rats took some time, 2 and 4 hours in Series I and III respectively, to begin their activity after the onset of darkness. This delay was not present in Series II where the animals became active soon after the onset of darkness, probably because they had enough rest during the long period of light. However, once they were active, they remained so for a period of 7 hours at one stretch.

The relationship of the mitotic activity to the body activity showed that when the duration of darkness was short, 7 hours/

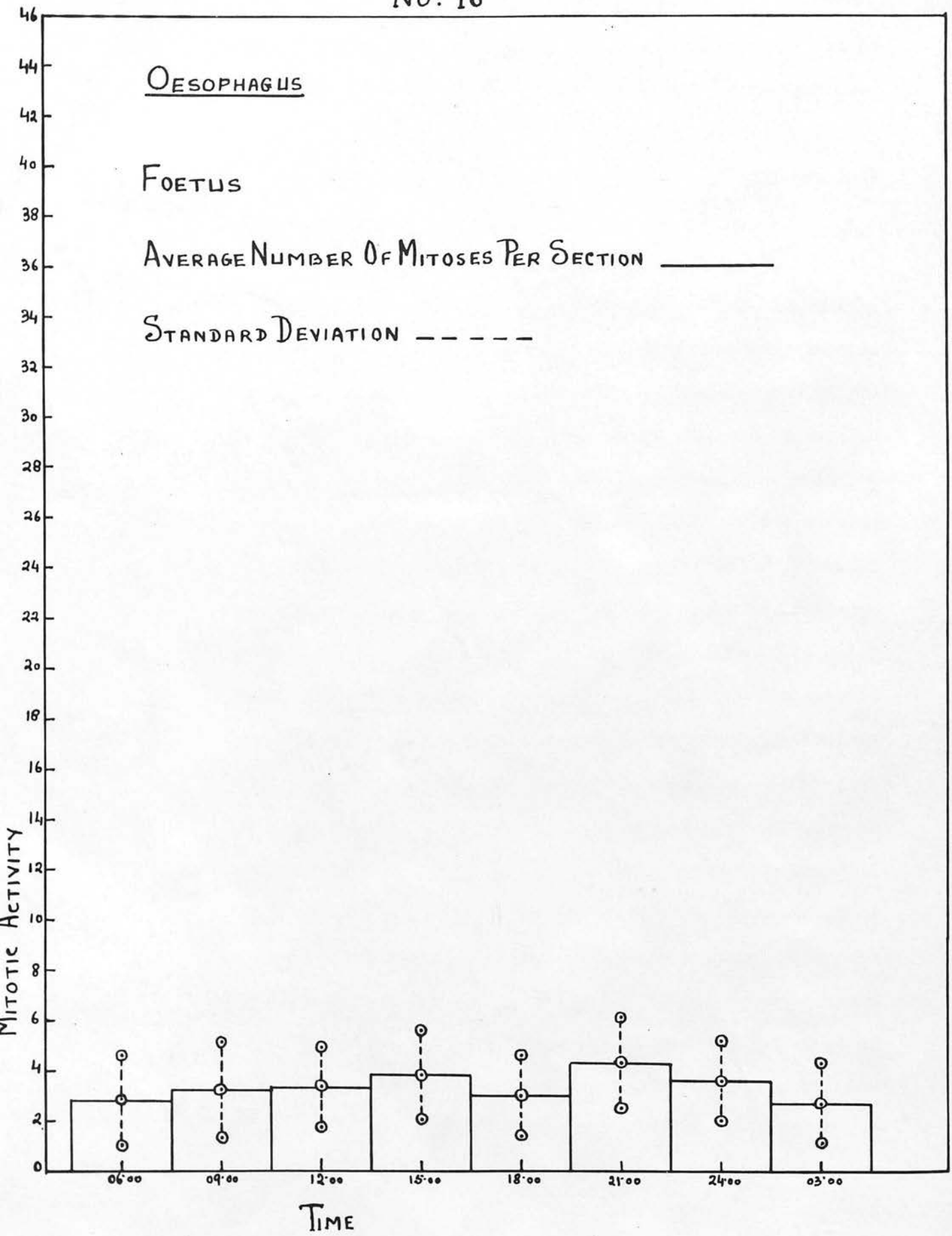
7 hours in Series II, the periods of high mitotic activity and high body activity clearly fell into the opposite halves of the 24-hour period. At the same time, it was found that the mitotic activity fell to a low value 5 hours before the rise in the body activity and the rise in the mitotic activity occurred 1 hour after the fall in the body activity. In the experiments where the animals were subjected to a longer period of darkness, as in Series I and III, and where the secondary period of high body activity was present, there was no evidence of a corresponding bimodality of the mitotic activity and the presence of the secondary period of high body activity appeared to have had no effect on the progress of the mitotic activity although it corresponded in time with the period when the mitotic activity was maximum. Clearly, in Series I and III also, the mitotic activity fell below the average 6 hours before the rise in the body activity, an interval similar to that found in Series II and the period of high mitotic activity began at the time when the primary phase of high body activity was waning, proceeded uninterruptedly during the secondary period of high body activity and remained above the average for 12 hours, 2 hours longer than in Series II where the periods of darkness and high body activity were both shorter. It was obvious from a comparison of the results in the first 3 series of experiments that the mitotic activity was in no definite relation to and was apparently unaffected by the body activity, except in so far as/

as it began in close relationship to the primary fall in the body activity; vide graph nos: 5, 9 and 21.

(Reversed Group)

In the reversed group of experiments, the most striking feature was that the single diurnal cycle of mitotic activity was completely reversed and so was the diurnal cycle of the body activity. The period of high mitotic activity maintained the same association with light and the period of low mitotic activity with darkness. The duration of high mitotic activity being 10 hours in Series IV and 12 hours in Series V. The 2 hours increase in Series V was probably only apparent and arose from the fact that the observations were taken at 4 hourly intervals. However, the duration of high mitotic activity was very similar to that observed in the control group of experiments where the animals were subjected to varying lengths of darkness. In addition, the rise in the mitotic activity followed the onset of darkness after an interval of 8 to 9 hours, 8 hours in Series V where observations had been recorded at 4-hourly intervals. These figures of 8 and 9 hours were very similar to that noticed in the control group; vide graph no: 19. It was further noticed that, as in Series II, there was a short period of darkness and the animals went into activity soon after the onset of darkness/

NO: 16


OESOPHAGUS
FOETUS
AVERAGE NUMBER OF MITOSES PER SECTION
STANDARD DEVIATION
MITOTIC ACTIVITY
46
44
42
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
06·00
09·00
12·00
15·00
18·00
21·00
24·00
03·00
TIME

darkness and remained so for a period of 9 hours, 1 hour more than that in Series II where duration of darkness (7 hours) was less than in Series IV and V (8 hours). However, the primary period of high body activity, in all the 5 series of experiments, was very similar. In relation to the short duration of darkness in Series IV and V, as in Series II, the periods of high mitotic activity and high body activity fell apart into the opposite halves of the 24-hour period and, like all other series, the mitotic activity fell to a low value 5 to 6 hours before the rise in the body activity and the rise in the mitotic activity occurred in close association with the falling body activity.

FOETUS GROUP

(Foetus Series)

Eight pregnant female rats, kept under standard conditions of natural lighting, were used for obtaining foetuses of 20 days. On the 20th day of pregnancy, one female rat was killed every 3 hours during a 24-hour period. 6 foetuses were taken out of each of them except in one case where only 4 foetuses were available. Mitotic activity, in the epithelium of the oesophagus, was studied for each sample of 6 foetuses and the average number of mitoses per section was recorded; vide table no: 10 and graph no: 16.

There/

There was no evidence of any periodicity in the mitotic activity in the course of 24 hours. The maximum rate of mitosis was seen to occur at 21.00 hours and the minimum at 03.00 hours. The difference between the rates of mitosis at these two hours was negligible and was not significant. The curve representing the mean values of the 8 samples was almost straight (graph no: 18).

(Mother Series)

Mitotic activity was also studied in the epithelium of the oesophagus of the 8 mothers and was expressed as the number of mitoses per section; vide table no: 11 and graph no: 17.

It was noticed that a periodicity, similar to that in male rats, occurred in the mitotic activity in the course of 24 hours, the maximum rate of mitosis being at 12.00 hours and the minimum at 18.00 hours. The difference between the two values was highly significant.

On comparison of the mitotic activity curve of the mother with that of the foetus, the former differed widely from the latter, due to the presence of the characteristic periodicity in the mitotic activity; vide graph no: 18.

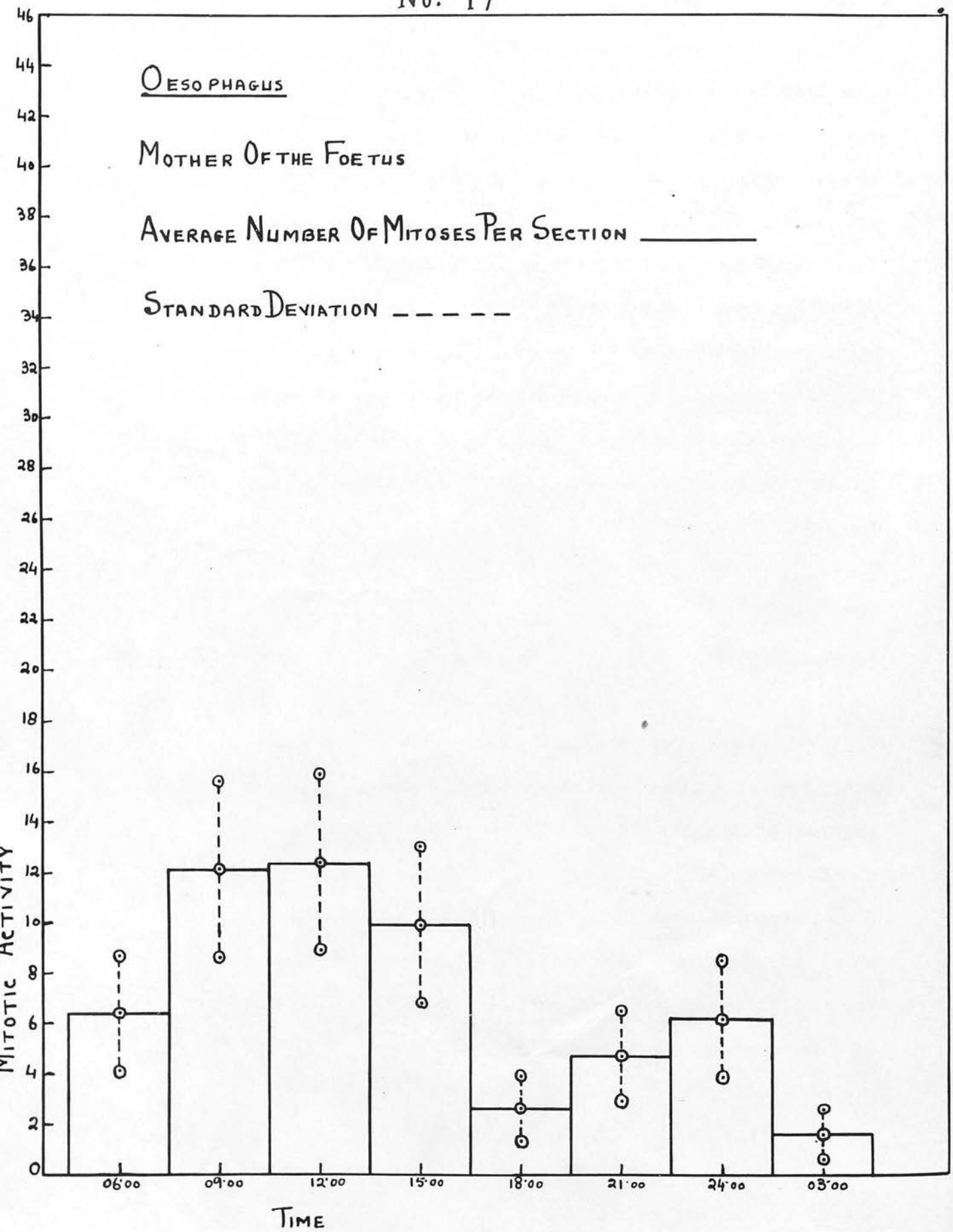
NO: 17

OESOPHAGUS

MOTHER OF THE FOETUS

AVERAGE NUMBER OF MITOSES PER SECTION _____

STANDARD DEVIATION - - - - -



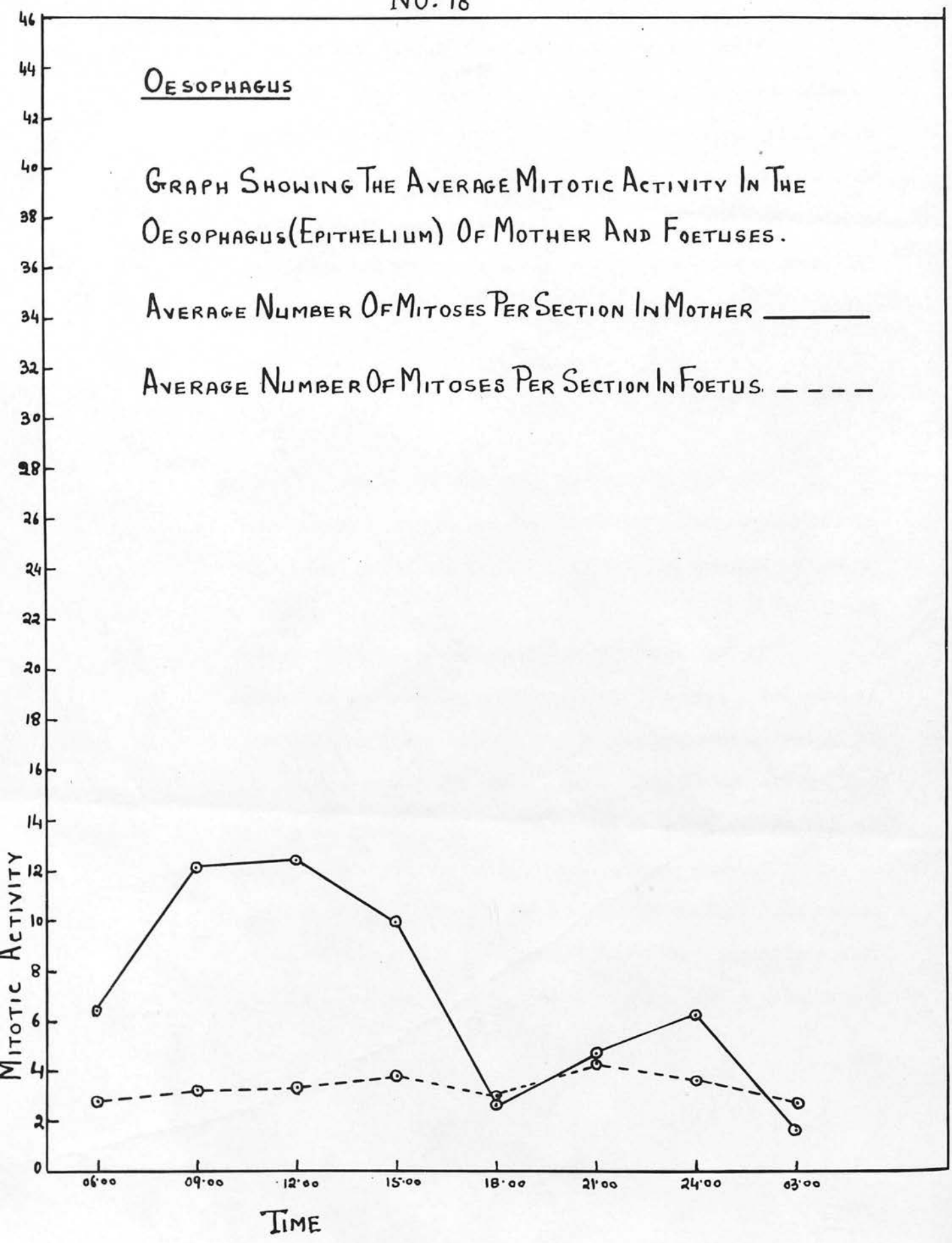
NO: 18

OESOPHAGUS

GRAPH SHOWING THE AVERAGE MITOTIC ACTIVITY IN THE OESOPHAGUS(EPITHELIUM) OF MOTHER AND FOETUSES.

AVERAGE NUMBER OF MITOSES PER SECTION IN MOTHER _____

AVERAGE NUMBER OF MITOSES PER SECTION IN FOETUS. - - - -



Foetus

Table showing the average mitotic activity per Section (10μ) in the Squamous epithelium of the Oesophagus of 36 foetuses (six obtained from one female rat), 6 being killed at 3 hourly intervals in the course of a 24 hour period.

Time	06.00	09.00	12.00	15.00	18.00	21.00	24.00	03.00
Mean No: of Mitoses per Section	2.8	3.2	3.3	3.8	3.0	4.3	3.6	2.7
S.D.	1.8	1.9	1.6	1.8	1.6	1.8	1.6	1.6
Variance	3.5	3.7	2.7	3.6	2.6	3.4	2.8	2.8
Range ·	0 to 9	0 to 10	0 to 7	0 to 9	0 to 7	0 to 10	0 to 9	0 to 7
Mother's No:	F7	F6	F1	F3	F4	F5	F2	F8

Table No: 10

Mothers of Foetuses

Table showing the average mitotic activity per Section (10^{M}) in the Squamous epithelium of the Oesophagus of 8 female rats (pregnant), one being killed at 3 hourly intervals in the course of 24 hours.

Time	06.00	09.00	12.00	15.00	18.00	21.00	24.00	03.00
Mean No: of Mitoses per Section	6.4	12.1	12.4	9.9	2.6	4.7	6.2	1.6
S.D.	2.3	3.5	3.5	3.1	1.3	1.8	2.3	1.0
Variance	5.3	12.7	12.6	9.9	1.7	3.3	5.7	1.2
Range	1 to 11	6 to 22	6 to 18	4 to 18	0 to 7	1 to 9	1 to 11	0 to 5
Rat No:	F7	F6	F1	F3	F4	F5	F2	F8

Table No: 11

D I S C U S S I O N

Several workers found variations both in the mitotic activity of different tissues and in the cyclical alterations which this activity showed. These were attributed to many variable factors such as age, sex, feeding time, diet, temperature, shock, stress, body activity and lighting conditions. Since the present work was an attempt to determine the nature of the mitotic cycle and the relationship, if any, which existed between the mitotic activity and the body activity or the lighting conditions, all other factors liable to cause variations in the results were eliminated as far as possible. It was believed that the habit of the rat was strongly affected, if not determined, by the diurnal variation in the temperature, the lighting conditions and time of feeding. As already mentioned, the temperature was maintained between 66° and 76°F and food was always available to the animals. It was found that the amount of food, eaten by the animals during the period of rest, was approximately equal to the amount of food eaten by them during the period of activity. Lighting conditions provided the only variable factor in the present work. This was primarily with the intention of determining whether any variation in the diurnal cycle of the mitotic activity resulted from changes in the lighting conditions and in what manner.

In/

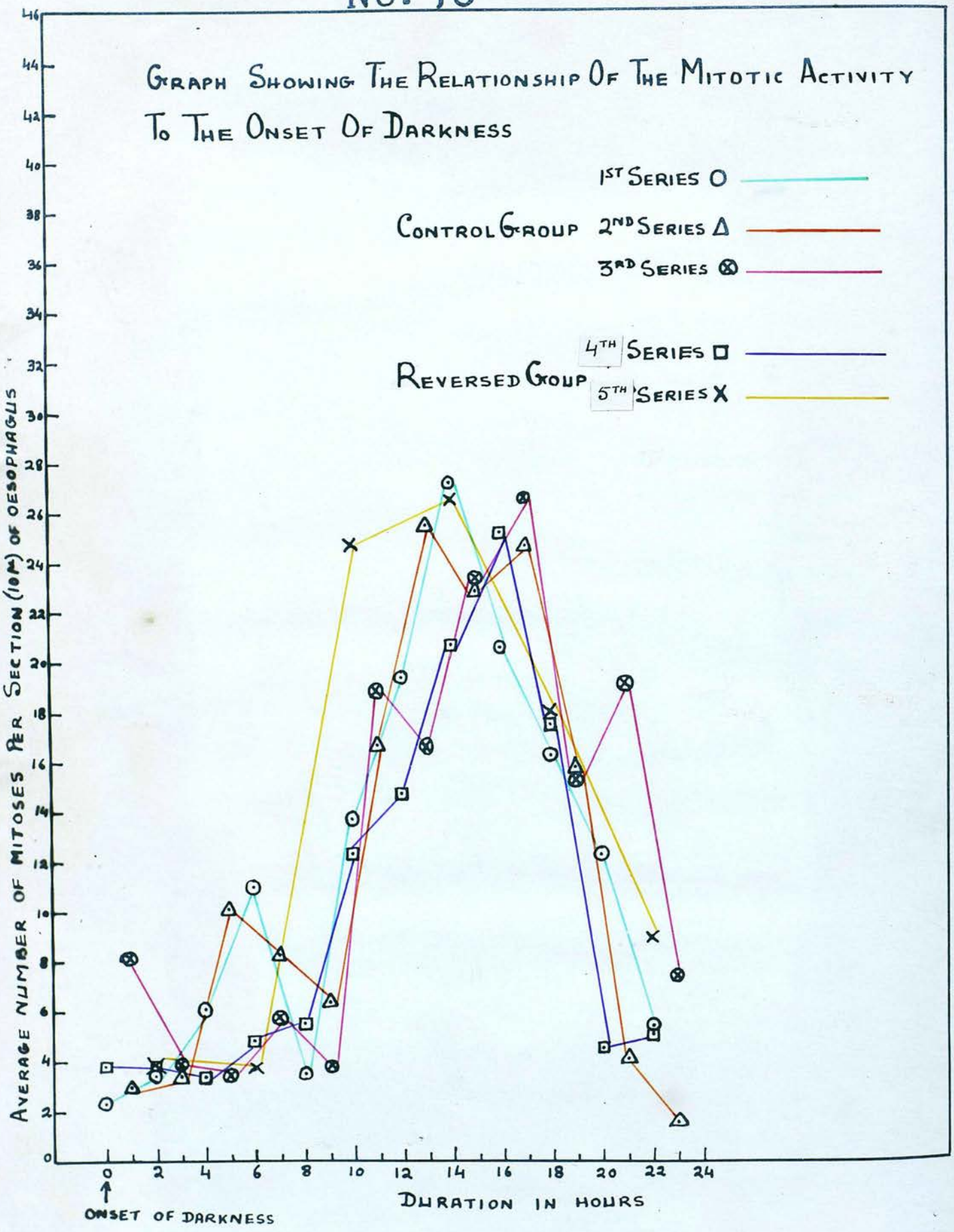
In the natural lighting conditions, the individual variation in the mitotic activity was enormous in contrast to that found in the artificial lighting conditions. A possible explanation, for this difference in the individual variation, might be that, in natural lighting, the onset of light or darkness was gradual and the rate of mitosis started to increase or decrease earlier in the rats, susceptible to the slightest change in the intensity of light. This would naturally cause a wide range of variation in the mitotic activity, at a given time, in different animals. On the other hand, in the case of artificial lighting, the change in the lighting conditions was sudden and if alterations in the intensity of light were the effective stimuli then it would be natural to expect that the mitotic activity would start simultaneously in all the animals which would, therefore, show a narrow range of variation at a given time. In view of a wide range of individual variation in the mitotic activity in the natural lighting conditions, it was not considered possible to determine, with accuracy, the exact hours of highest and lowest mitotic activity and significance was attached only to a period characterised by a high rate of mitosis in consecutive samples and a period characterised by a low rate of mitosis in the consecutive samples. In series I and II, there was a suggestion of a rise in the rate of mitosis towards the end of the period of low mitotic activity. This rise in the rate of mitosis/

mitosis did not appear to be significant in view of the enormous individual variation, already referred to, in the natural lighting conditions. Such a rise in the mitotic activity did not occur in series III, IV and V where the animals, exposed to artificial lighting conditions, exhibited a narrow range of individual variation in the rate of mitosis. Nevertheless, it was surprising that the only marked indication of the individual variation, if this was indeed what it was, should have occurred at the same phase of the mitotic cycle in both series of experiments. However, in view of the above considerations and the fact that this rise in the rate of mitosis was found to be less than the value for the average mitotic activity in the course of 24 hours, it was considered fairly reasonable to include such a rise in the mitotic activity within the period of low mitotic activity.

The outstanding feature of the present work, with regard to the diurnal variation in the mitotic activity in the oesophageal epithelium of the rat, was that, in spite of a considerable individual variation, there existed a clearly defined single diurnal cycle of mitotic activity. In spite of considerable variation in the lighting conditions and in the activity of the animals, the pattern of the mitotic cycle was constant, a high rate of mitosis occurring for a period of 10 to 12 hours and a low rate of mitosis for a period of 12 to 14 hours. The high rate of mitosis tended to be associated/

associated with the periods of light and low body activity while the low rate of mitosis tended to be associated with the periods of darkness and high body activity. The relationship of the mitotic cycle to the lighting conditions and the activity of the animals was only a general one because the period of high mitotic activity did not bear a strict association either with the duration of light or low body activity, and the period of low mitotic activity bore no strict association either with the duration of darkness or high body activity. This evidence appeared to indicate that the mitotic cycle was independent of the lighting conditions and the activity of the animals. But the evidence, with regard to the reversal of the diurnal cycle of the mitotic activity in the reversed lighting conditions, not only ruled out the possibility of a completely independent mitotic cycle but also indicated that, in the conditions in which the animals were kept, the mitotic cycle was dependent either on the lighting conditions or on the activity of the animals or on both. This view was extended with good reason in view of the fact that the mitotic cycle was reversed in the reversed lighting conditions and that, even in this condition, it bore a general relation to the lighting conditions and the activity of the animals, similar to that found in the control groups of experiments. The present work showed that, though the relationship between the mitotic activity and the body activity or the lighting conditions was only a general one, there were two constant features/

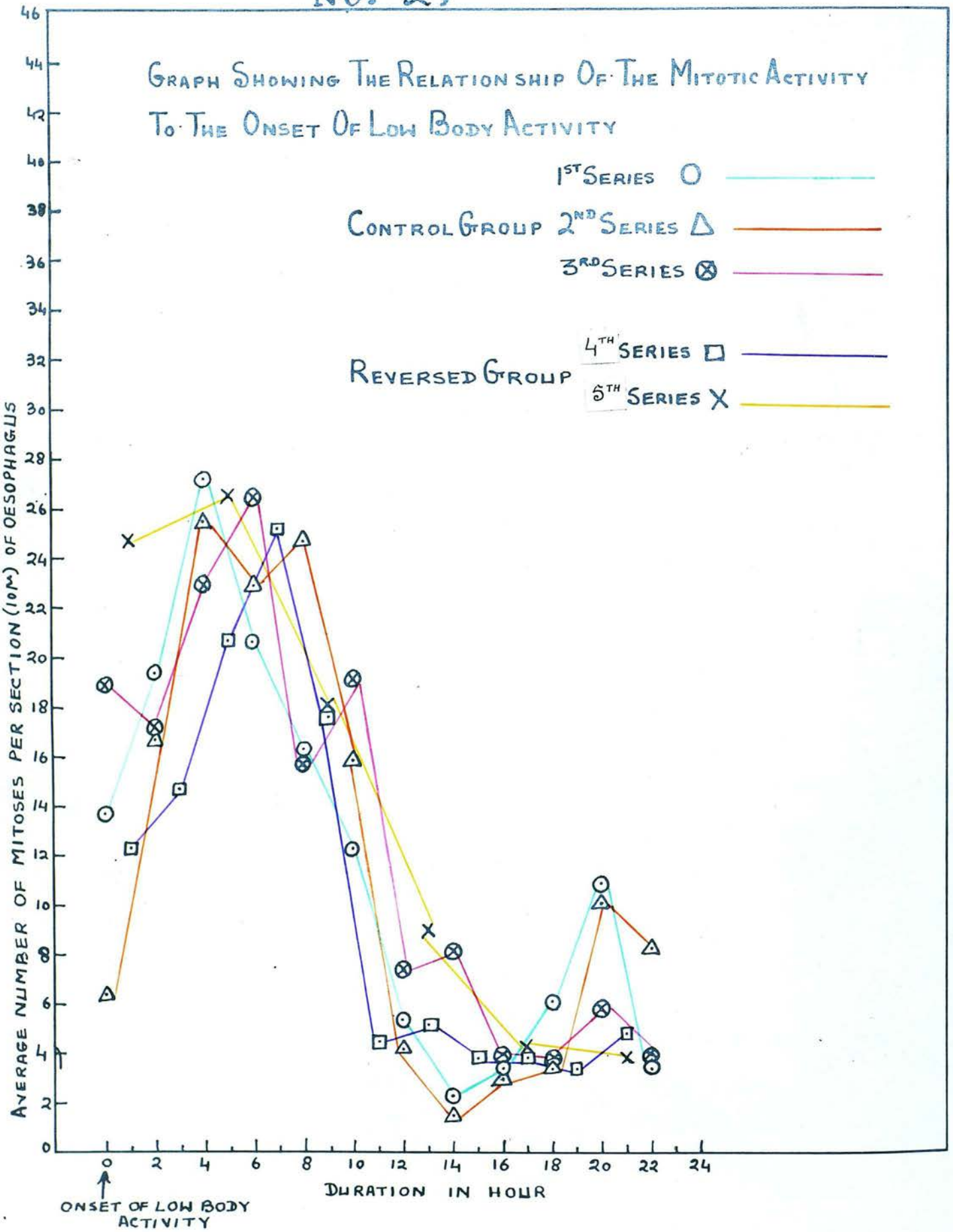
NO: 19



Graphs of all series were superimposed to show that the rise in the mitotic activity occurred 8 to 10 hours after the onset of darkness.

features in all the series of experiments. First, the rise in the mitotic activity occurred 9 to 10 hours after the onset of darkness (graph No: 19) and second, it was closely associated with the primary fall in the body activity (graph No: 21). In view of these constant features, there were two possible explanations for the rise in the rate of mitosis in the diurnal cycle of the mitotic activity: (1) The primary fall in the body activity initiated the rise in the rate of mitosis which, once raised, became independent of the body activity and continued uninterruptedly for a period of 10 to 12 hours. This view was suggested because of the close association of the rising mitotic activity with the falling body activity (primary) and the absence of evidence of a rise in the rate of mitosis corresponding to the secondary fall in the body activity (series I and III), and the simultaneous existence of low mitotic activity and low body activity for a period of about 5 hours at the end of the period of high mitotic activity; (2) The onset of darkness initiated the rise in the mitotic activity after an interval of 9 to 10 hours. Once the mitotic activity was raised, it became independent of the lighting conditions and continued at a high level for a constant period of 10 to 12 hours. Thus it seemed likely that either one or both of the above factors were responsible for the increased mitotic activity and that, if so, they must be responsible solely for its initiation. Whichever of the two factors/

NO: 21



Graphs of all series were superimposed to show the close association of the rise in the mitotic activity with the primary fall in the body activity.

factors initiated the rise of the mitotic activity, it possibly did so through some intermediary substance in the blood. If it was so, there should have been a variation of the mitotic activity in the foetus unless the foetal tissue behaved in a different manner or the placenta was not permeable to this hypothetical substance.

The findings of Karsten (1915) and Stalfelt (1921), in plants, supported the present work with regard to the single cycle in the mitotic activity during a period of 24 hours. Kellicott (1904), however, found two maxima in the mitotic activity in Allium. As suitable data about the conditions in plants were not available in the present work, it was not possible to give any explanation for the difference between the findings of the above workers with regard to the time of maximum mitotic activity and the number of maxima in the course of 24 hours. Karsten (1918) failed to notice any periodicity in the rate of mitosis, in buds of various plants, in conditions of continuous exposure to light and Fortuyn-van Leijden (1926) found a rhythmical cell division, different from the diurnal periodicity, in the root tips of Allium cepa with alternating maxima and minima in conditions of continuous darkness. These findings suggested that darkness was essential for the rhythmic character of the mitotic activity in the plants. Berinsohn (1919) found darkness to be associated with increased mitotic activity because he noticed that Allium root/

root tips contained more karyokinetic figures after a period of exposure to darkness than after a similar exposure to light. In other experiments, Fortuyn-van Leijden (1926) found that illumination during day time changed the rhythmic nature of the mitotic activity in the root tips of allium cepa, noticed during continuous exposure to darkness, into a daily periodicity with the largest number of mitoses during the period of darkness. This change to the diurnal periodicity of the mitotic activity might have been due to the influence of light in the diurnal cycle of day and night. But, according to Karsten (1918), light by itself could not be responsible for the diurnal periodicity in the mitotic activity. The above workers examined the relationship of the lighting conditions to the mitotic activity in the root tips which were not in their normal condition as, in fact, they normally remain under ground and are not exposed to light. However, it appeared from their observations that alternating light and darkness was associated with a diurnal periodicity of the mitotic activity in plants.

The investigation, on human epidermis, by Cooper and Schiff (1938) was limited to a few scattered observations and that by Broders and Dublin (1938) was limited to hourly observations from 7 a.m. to 1 a.m. In view of the fact that their findings did not consist of the study of the mitotic activity throughout a complete period of 24 hours, it was not possible/

possible to ascertain whether a single or a double cycle of the mitotic activity existed in human tissue. However, it appeared from their report that, in human tissue also, there existed a single diurnal cycle in the mitotic activity, a high rate of mitosis occurring during the period of darkness and a low rate of mitosis during the period of light. The present work, on rats, agreed with the above findings so far as the single cycle of the mitotic activity was concerned but differed in view of the time of high and low rates of mitosis. Such a difference might be due to the fact that, in contrast to human beings, the rats were nocturnal in their habits. In view of the absence of any definite data regarding the activity of the infants and the possibility that the infants, a few days old, could be restful or active at any time of day or night, it was not possible to attribute the above difference in the mitotic activity to the difference in the habits of infants and rats. Among other explanations which might have been put forward to explain the difference in the time at which the high mitotic rate occurred in infants and rats was that, due to the diurnal nature of the infants, the rise in the rate of mitosis occurred as a result of the stimulus received from the onset of light; whereas the effective stimulus to the body activity, at any rate, was the onset of darkness in the nocturnal animals.

The findings of Fortuyn-van Leijden (1917), on 2-day old/

old kittens, supported the present work with regard to the single diurnal cycle of mitotic activity. In view of the fact that the diurnal variation in the mitotic activity was not present in the rat foetus (present work) and presumably was in the process of development in the neonatal phase, and that the pattern of the mitotic activity was known to vary at different ages (Bullough 1949), and that the cat was a less strictly nocturnal animal than the rat, it was not surprising that the findings of Fortuyn-van Leijden, with regard to the time of high and low mitotic activity in 2-day old kittens, differed from the present findings on adult rats. As regards the relationship of the mitotic activity to the body activity of the kittens, it was not possible to draw any conclusion because Fortuyn-van Leijden did not give any data concerning the activity of the animals and nothing definite could be inferred as the kittens were only 2 days old. However, the explanation for the disagreement with the present work could have been that the mitotic activity progressed differently in kittens and rats due to the difference in their body activity and this the more so because alterations in the lighting conditions were probably less effective in recently born kittens in which the eyes were still closed.

In view of the absence of information regarding the individual variation in the mitotic activity in the works of Fortuyn-van Leijden (1926) and Carleton (1934), on mice, significance/

significance was not attached to the exact hours of maximum and minimum mitotic activity. They agreed with the present work so far as the single cycle of the mitotic activity was concerned but, with regard to the time of high and low mitotic activity, only Fortuyn-van Leijden agreed with the present findings and not Carleton, who found a high rate of mitosis during the period of darkness and a low rate of mitosis during the period of light, though the age of the animals was almost the same (8 hours to 2 weeks) in the experiments of both workers. Since the periodicity in the mitotic activity, in the rat foetus, was not found in the present work, it was apparent from the above results that the mitotic cycle began some time shortly after birth and that either the lighting conditions or the body activity or both were instrumental in the production of such a cycle. The difference between the findings of Fortuyn-van Leijden and Carleton might be attributed to the difference in the body activity because the activity of the animals, as young as those used by these workers, was liable to be variable due to disturbance caused by the mother while feeding and other processes of like nature. Naturally, in those circumstances, a variation in the time of high and low mitotic activity was not unexpected, especially as the cyclical variation in the mitotic activity was in the process of development.

The findings of Cooper and Franklin (1940), on mouse epidermis,/

epidermis, and of Blumenfeld (1938 and 1939), on the epidermis and the renal cortex of rats, supported the present work regarding the pattern of the mitotic cycle. In addition, they agreed with the present findings with regard to the general relationship of the mitotic cycle to the lighting conditions. Since none of these workers gave a detailed account of the lighting conditions or the activity of the animals, it was not possible to make any definite correlation between the mitotic activity and the lighting conditions or the body activity. However, by way of inference, it was assumed that, since the rats and mice were nocturnal animals, they might have been active during the night and restful during the day. If this inference was accepted, then it followed that the mitotic activity bore a general inverse relationship to the body activity. The absence of the diurnal variation in the mitotic activity, in the submaxillary salivary gland noticed by Blumenfeld (1942) and in the proliferation centres of intestinal lymph nodules and seminiferous tubules of the testes found by Bullough (1947), suggested that, whatever factor or factors determined the periodicity in the mitotic activity, it had a selective influence so as to cause periodicity in the mitotic activity in certain organs and not in others. The present work agreed with the findings of Blumenfeld (1943), on mouse epidermis, with regard to the nature of the mitotic cycle and the time at which high and low mitotic activity occurred./

occurred. Though Blumenfeld gave no details concerning the activity of the animals, mitotic activity, by way of inference, bore a general inverse relationship to the body activity. Blumenfeld (1944) found that the mitotic activity in the renal cortex, at a given time, was inversely related to the volume of urine excreted during the preceding 6 hours and the mitotic activity in the submaxillary salivary gland, at a given time, was inversely related to the amount of food eaten during the preceding 6 hours. From these observations, he concluded that the mitotic activity, in the renal cortex and the submaxillary salivary gland, was inversely related to the work done by the cells of these organs. It appeared that his conclusion was not justifiable in view of the fact that the time during which the urine was excreted or the food eaten, was different from that at which the mitotic activity was studied. Moreover, with regard to his experiments on the renal cortex, his assumption , that a large volume of urine (diluted) indicated more work done by the cells of the renal cortex and a small volume of urine (concentrated) indicated less work done by those cells, appeared to be opposed to what would be expected in those circumstances.

Bullough (1947) differed from the present work with regard to the pattern of the mitotic cycle. He found a double cycle of the mitotic activity in the ear epithelium of the mouse. He also demonstrated a similar cycle of mitotic activity/

activity in other organs of the mouse such as mid-dorsal epidermis of the back, epithelium of the oesophagus, lining epithelium of the epididymis and the proliferating zone of the duodenal mucosa. None of the previous workers found such a double cycle in the diurnal variation of the mitotic activity in rats or mice and in the present work also, there was no evidence of such a cycle of the mitotic activity in the oesophageal epithelium of the rat. As an explanation for the difference of his results from that of other workers, Bullough (1947) said that, since the mitotic cycle, in the mouse, was entirely dependent on the activity of the animals in the course of 24 hours, the pattern of the mitotic cycle was likely to vary from animal to animal corresponding to the variation in the body activity. As already mentioned, Bullough (1947) found that the mitotic activity, in the mouse, bore a strict inverse relationship to the body activity. In addition, Bullough (1947) experimentally induced rest and exercise in mice and found that the mitotic activity was high during the period of rest and low during the period of activity. The mechanism which controlled this relationship was considered, by Bullough (1948) and Bullough and Eisa (1950), to be the deposition of glucose, as glycogen, in the tissues during the period of rest. The presence of the glycogen was thought to be a critical factor for the rise in the rate of mitosis. On the other hand, during the period of exercise, the/

the tissue glycogen was withdrawn in the blood, in the form of glucose, thereby leading to a fall in the rate of mitosis. The present work, on the rat, showed that the mitotic activity bore only a general inverse relation to the body activity. It was admitted that only 4 out of 12 rats of a series were used for the study of the body activity and that this fact might have introduced a slight error in the hourly figures representing the body activity of the 12 rats in the course of 24 hours. But in view of the fact that, during the day, each figure in the 24-hour body activity curve for each series represented the average of 20 observations and, during the night, it represented the average of 2 observations, any major error in the pattern of the body activity curve was unlikely. On comparison of the mitotic cycle and the body activity, in the present work, it was found that, besides the close association of the rise in the mitotic activity with the primary fall in the body activity, there was always a period of about 5 hours, at the end of the period of high mitotic activity, when the mitotic activity and the body activity were found to be low in all the experiments irrespective of the variations in the lighting conditions. In addition, when the period of darkness was long as in series I and III, there was a secondary interval of high body activity which coincided in time with high mitotic activity. These features hardly indicated that the mitotic activity always bore a strict inverse relationship to/

to the activity of the rats. In view of the theory extended by Bullough and Eisa (1950) and the fact that glucose from the maternal circulation passed freely, through the placental barrier, to the foetal circulation (Huggett, 1954), it was reasonable to assume that there would be a diurnal variation of the mitotic activity in the foetal tissue corresponding to the maternal cycle, provided that the same factors applied to the foetus as to the mother. But evidence, from the present work on the foetus, did not show any variation in the mitotic activity although the characteristic single diurnal cycle of the mitotic activity was present in the mothers. A possible explanation could be that the above theory was not applicable to the foetus where the mitotic activity was possibly concerned only with growth and not with replacement of the worn out tissues.

Laws (1952) disagreed with the theory of Bullough and Eisa (1950) because he did not find any change in the blood sugar level of the tumor-bearing mouse. This observation led him to think that the progressive depression of epidermal mitosis that developed in the tumor-bearing mouse could not be attributed to any inadequacy in the supply of carbohydrate to these cells. There were, however, other complicating features to be taken into account in pathological conditions and it might be that Laws' criticism was not completely valid.

Blumenthal/

Blumenthal (1940) did not think that the lighting conditions played an important role in the determination of the mitotic cycle because he found that a rise in the rate of mitosis could be brought about at any time of day or night depending upon the time of feeding and subsequent metabolic processes. In view of the fact that the food given to the animals lasted for only one hour after the feeding time, it was evident that the animals were in a comparative state of underfeeding. Mitotic activity, in such conditions, was liable to be depressed markedly (Bullough, 1949). Feeding at a particular time, in such circumstances, might have influenced the mitotic activity either directly or through the medium of a change in the pattern of the body activity of the underfed animals and thus led him to believe that, normally, feeding time was the important factor in the determination of the mitotic cycle. In contrast to Blumenthal's findings, the present work showed that a single diurnal cycle of the mitotic activity was present in the rat though the animals were fed twice daily, morning and evening.

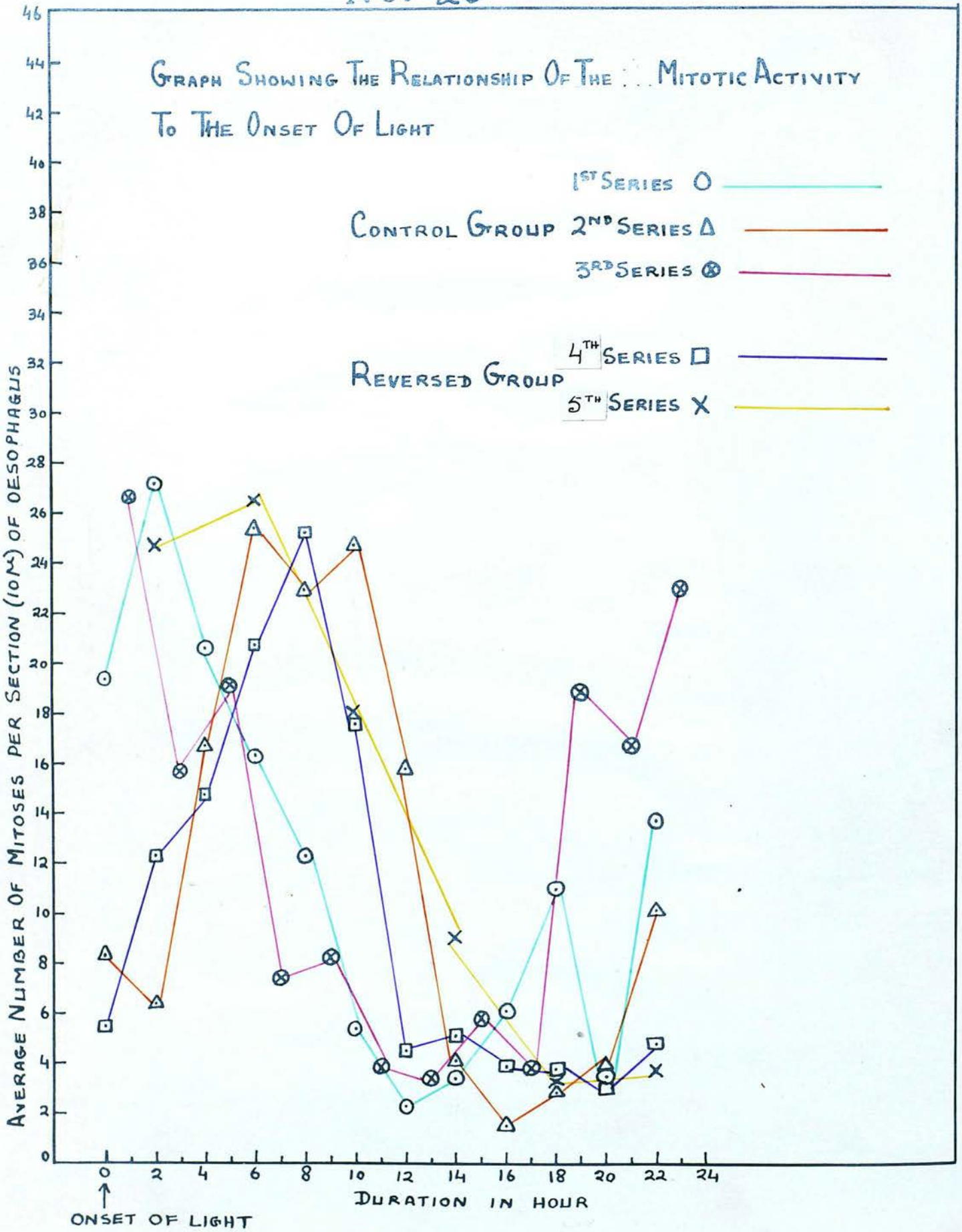
Though the review of the literature showed that many of the previous workers did not study the relationship of the mitotic activity to the body activity of the animals, it was believed, by way of inference, that the mitotic activity bore an inverse relation to the body activity. Some of them, however, did examine the relationship of the mitotic activity to the/

the lighting conditions in plants and animals. From the evidence in their reports, it appeared that the lighting conditions played an important role in the causation of the periodic character of the mitotic activity. Since necessary data were not available in their reports, it was not possible to find out the exact nature of the relationship between the mitotic activity and the lighting conditions. Bullough(1947) was the only worker who studied the relationship between the mitotic activity and the body activity of the mouse. His findings, with regard to the general relationship between the mitotic activity and the body activity, agreed with the present work. But Bullough's findings differed from that found in the present work in view of the fact that he noticed a double diurnal cycle of the mitotic activity and that the mitotic activity bore a strict inverse relation to the body activity. However, it appeared, from the observations of the previous workers, that the evidence in favour of the relationship between the lighting conditions and the mitotic activity was almost similar to that in favour of the relationship between the body activity and the mitotic activity. This was in keeping with the present findings where both the onset of darkness and the primary fall in the body activity bore a constant temporal relationship to the rise in the mitotic activity.

With regard to the factors which controlled the

duration/

No: 20



Graphs of all series were superimposed to show that the onset of light had a very variable relationship to the mitotic activity.

duration of the high mitotic activity or determined the fall of the mitotic activity at the end of 10 to 12 hours, it was not possible to come to any definite conclusion. The onset of light bore a very variable relation to the mitotic activity (graph No: 20) and could not be considered to have any definite relation to the duration of high mitotic activity. On the basis of the evidence that the mitotic figures were invariably situated in the basal layer of the oesophageal epithelium (present work), that a cell took about 2 to 3 hours to undergo mitosis (Bullough, 1950), and that the intermitotic period varied from 8 to 18 hours (Fell and Hughes, 1949), the duration of high mitotic activity might be restricted to 10 to 12 hours if almost all the cells of the basal layer had undergone mitosis in that period. This explanation could be valid if the average number of cells per section in the basal layer was, if not akin, not greatly different from the average number of the mitotic figures encountered in the course of 24 hours. The observations, in the present work, ruled out the above explanation because the average number of the cells in the basal layer was estimated at 1153 (table 1) and the average number of the mitotic figures observed in the course of 24 hours was approximately 250.

It was assumed that, if all the animals followed a similar course, the sum of the average figures for mitoses per section in all the samples from one series would give an estimate/

estimate of the total number of mitoses in a 24-hour period. This figure would, in all probability, exceed the real number since the time taken to complete an individual mitosis (2 to 3 hours) was longer than the interval between the samples (2 hours). Thus the figure of 250 is probably a liberal estimate. Again, since the figures for the duration of the inter-mitotic period of cells growing in tissue culture was 8 to 18 hours, and if these figures were applicable to the intact rat, then it was unlikely that any one cell would undergo mitosis more than once in a 24-hour period. Hence the figure of 250 probably represented the number of different cells undergoing mitosis in the course of 24 hours. The disparity between the average number of cells in the basal layer of the oesophageal epithelium and the average number of mitoses observed in 24 hours indicated that at most, one fourth of the total number of cells in the basal layer entered mitosis during a 24-hour period. If the onset of darkness or the primary fall in the body activity, as found in the present work, provided the stimulus for the rise in the mitotic activity, why was it that only this small number (250) of cells entered the process of cell division? In addition, it was known that a cell took about 2 to 3 hours to divide, yet the duration of high mitotic activity was 10 to 12 hours; this made it appear that certain cells started to divide early whereas others followed after a fairly long interval. Here again, if the onset of darkness

or/

or the primary fall in the body activity acted as a stimulus to initiate the rise in the mitotic activity, why was it that some cells were activated at the beginning of the period of high mitotic activity whereas others were not so affected until the latter part of the period of high mitotic activity? A probable answer to these questions might be that the onset of darkness or the primary fall in the body activity caused the release of some mitosis stimulating substance which was in circulation for a period of 10 to 12 hours. Whatever this substance might have been, the evidence produced here on the foetal mitotic rate suggested that it did not pass the placental barrier or was ineffective on the foetal tissue. The other possibility could have been that the onset of darkness or the primary fall in the body activity released the cells from the normal inhibition which controlled excessive mitotic activity and thereby facilitated the increase in the mitotic activity.

In view of the available evidence in the present work, it was suggested that probably the onset of darkness or the primary fall in the body activity or both were responsible for the rise in the rate of mitosis which, once raised, became independent of the lighting conditions and the activity of the animals and continued to be high for a constant period of 10 to 12 hours. Further work on this problem was needed to dissociate the high body activity from darkness and the low body activity from light./

light. Only then, could it be possible to throw more light on the factor or factors governing the mitotic cycle. Dissociation of the body activity from the lighting conditions might be brought about by keeping the animals either in continuous darkness or in continuous light.

S U M M A R Y

Mitotic activity was studied in the oesophageal epithelium of adult male rats and 20 day old foetuses with special reference to the diurnal variation and its relationship to the lighting conditions and the activity of the animals. The animals were kept in standard conditions and all factors liable to cause variation in the results were eliminated as far as possible.

For the investigation of the problem, the animals were divided into 4 groups. Control Group: out of 36 rats of this group, 24 rats, of the first 2 series, were kept under natural lighting conditions and the 12 rats, of the 3rd series, were kept under artificial lighting conditions for a period of 90 days (light during the day and darkness during the night). Reversed Group: 18 rats of this group, 12 rats of the 4th series and 6 rats of the 5th series, were exposed to light during the night and to darkness during the day for a period of 90 days. At the age of 120 to 130 days, the rats of all the 5 series were sacrificed, one from each series at 2-hourly intervals in the course of 24 hours, except series V where the interval was 4 hours. The mitotic activity was expressed as the number of mitoses per section of the oesophagus (10 μ). Individual Variation Group: 12 rats, kept under natural lighting conditions, and 6 rats, kept under artificial lighting/

lighting conditions, were sacrificed at a time when a high rate of mitosis was expected and the individual variation in the mitotic activity was studied. Foetus Group: 6 foetuses, from one pregnant female rat, were examined at 3-hourly intervals in a 24-hour period, making 48 foetuses in all and the average mitotic activity was determined for each sample of 6 foetuses. In addition, the mitotic activity was studied in the oesophageal epithelium of the pregnant female rats corresponding in time with each sample of foetuses.

The important finding which emerged from the observations was that, in spite of considerable individual variation, there existed a clearly defined single cycle of mitotic activity in the oesophageal epithelium of the adult male rat. The observations indicated that, in the conditions in which the animals were kept, high mitotic activity tended to occur during the period of light when the body activity was low and low mitotic activity tended to occur during the period of darkness when the body activity was high. The period of high mitotic activity varied from 10 to 12 hours and the period of low mitotic activity varied from 12 to 14 hours. The other important feature was that, with the reversal in the lighting conditions, the single cycle of the mitotic activity was completely reversed but maintained its position relative to the lighting conditions and the activity of the animals, similar to that observed in the control groups of experiments. The

body/

body activity was also reversed so that the period of high body activity continued to fall in the period of darkness. With regard to the exact nature of the relationship of the mitotic activity to the lighting conditions or the activity of the animals, two constant features were noticed in all series of experiments. Firstly, the rise in the mitotic activity occurred 9 to 10 hours after the onset of darkness, secondly, the rise in the mitotic activity was closely associated with the primary fall in the body activity. It was believed that either one or both of these factors initiated the rise of the mitotic activity which, once raised, became independent of the lighting conditions and the activity of the animals and proceeded uninterruptedly for a constant period of 10 to 12 hours. In a general way, a high rate of mitosis was related to light and low body activity and a low rate of mitosis was related to darkness and high body activity. Such a relationship was more distinct in series II, IV and V where the duration of darkness was short and the period of high mitotic activity was confined to the period of light and associated with low body activity. As the duration of darkness increased, as in series I, a part of the period of high mitotic activity fell in the period of darkness and coincided with the secondary rise in the body activity. With a further increase in the duration of darkness, as in series III, half of the period of high mitotic activity fell in the period of darkness and coincided with a protracted/

protracted secondary interval of high body activity. In the case of the foetus, there was no evidence of a diurnal variation in the mitotic activity. In contrast to this, the characteristic single cycle of the mitotic activity, similar to that in adult male rats, was present in the pregnant female rats from which the foetuses were obtained.

The above observations were discussed with the findings of other workers and it was found that there was a fair agreement with regard to the relationship of high mitotic activity to the period of light and low body activity and of low mitotic activity to the period of darkness and high body activity. As regards the probable factor or factors responsible for the determination of the mitotic cycle, it was suggested that the onset of darkness or the primary fall in the body activity or both acted as a stimulus for the rise in the mitotic activity which, once raised, became independent of the lighting conditions and the activity of the animals and continued for a constant period of 10 to 12 hours. Whatever was the factor which controlled the mitotic cycle in the oesophageal epithelium of the adult rat, it was ineffective in the case of the foetus.

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APPENDIX

Individual variation Group (Natural lighting Conditions)

Rat No: 48

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	26	11
2	11	27	6
3	13	28	8
4	9	29	7
5	11	30	13
6	7	31	11
7	7	32	7
8	5	33	3
9	10	34	7
10	8	35	4
11	4	36	8
12	6	37	6
13	10	38	7
14	11	39	3
15	10	40	5
16	5	41	6
17	12	42	7
18	9	43	4
19	10	44	10
20	3	45	4
21	10	46	6
22	4	47	5
23	5	48	8
24	7	49	10
25	7	50	8

Mean 8.0

S.D. 2.7

Variance 7.3

Range 3 to 13

Rat No: 49

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	10	26	13
2	14	27	11
3	19	28	17
4	18	29	11
5	13	30	21
6	30	31	21
7	12	32	11
8	19	33	17
9	19	34	14
10	8	35	19
11	16	36	16
12	11	37	18
13	7	38	15
14	17	39	10
15	15	40	14
16	14	41	15
17	21	42	10
18	20	43	14
19	14	44	20
20	14	45	10
21	14	46	9
22	15	47	21
23	16	48	23
24	13	49	15
25	19	50	10

Mean 15.8

S.D. 4.4

Variance 20.0

Range 7 to 30

Individual variation Group (Natural lighting Conditions)

Rat No: 47

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	11	26	18
2	8	27	16
3	15	28	12
4	17	29	23
5	21	30	13
6	19	31	15
7	13	32	19
8	12	33	15
9	15	34	15
10	19	35	10
11	9	36	15
12	14	37	10
13	17	38	17
14	17	39	16
15	8	40	13
16	10	41	14
17	16	42	9
18	11	43	20
19	18	44	21
20	9	45	11
21	19	46	14
22	19	47	13
23	12	48	20
24	15	49	15
25	18	50	17

Mean 15.4

S.D. 3.7

Variance 14.2

Range 8 to 23

Rat No: 56

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	6	26	7
2	8	27	2
3	9	28	10
4	15	29	8
5	10	30	8
6	6	31	3
7	9	32	6
8	11	33	6
9	10	34	11
10	14	35	11
11	6	36	5
12	8	37	10
13	7	38	8
14	7	39	5
15	6	40	8
16	9	41	8
17	8	42	7
18	7	43	4
19	6	44	9
20	8	45	10
21	5	46	9
22	4	47	11
23	8	48	7
24	3	49	9
25	6	50	8

Mean 8.3

S.D. 2.5

Variance 6.6

Range 2 to 15

Individual variation Group (Natural lighting Conditions)

Rat No: 45

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	12	26	9
2	24	27	11
3	18	28	20
4	10	29	12
5	14	30	12
6	12	31	14
7	13	32	9
8	12	33	10
9	15	34	14
10	15	35	9
11	10	36	9
12	11	37	6
13	13	38	15
14	11	39	2
15	15	40	7
16	4	41	6
17	10	42	15
18	16	43	11
19	11	44	14
20	10	45	10
21	17	46	10
22	14	47	4
23	11	48	12
24	6	49	9
25	12	50	7

Mean 12.0

S.D. 4.0

Variance 16.4

Range 2 to 24

Rat No: 46

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	16	26	1
2	8	27	6
3	7	28	6
4	8	29	7
5	9	30	10
6	12	31	7
7	11	32	12
8	12	33	11
9	14	34	13
10	3	35	12
11	4	36	10
12	4	37	7
13	5	38	7
14	8	39	9
15	15	40	7
16	16	41	10
17	9	42	10
18	7	43	12
19	9	44	10
20	7	45	4
21	11	46	11
22	13	47	7
23	7	48	4
24	11	49	8
25	7	50	7

Mean 9.4

S.D. 3.3

Variance 11.0

Range 1 to 16

Individual variation Group (Natural lighting Conditions)

Rat No: 50

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	6	26	5
2	4	27	4
3	9	28	3
4	5	29	5
5	11	30	10
6	10	31	7
7	5	32	11
8	11	33	5
9	8	34	4
10	3	35	6
11	9	36	8
12	6	37	4
13	3	38	6
14	8	39	7
15	7	40	5
16	2	41	10
17	7	42	4
18	7	43	8
19	6	44	7
20	4	45	7
21	5	46	4
22	5	47	4
23	8	48	3
24	6	49	9
25	6	50	5

Mean 6.8

S.D. 2.3

Variance 5.6

Range 2 to 11

Rat No: 51

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	15	26	12
2	14	27	11
3	11	28	13
4	11	29	23
5	13	30	17
6	17	31	13
7	22	32	10
8	13	33	13
9	18	34	12
10	17	35	11
11	16	36	10
12	14	37	21
13	18	38	12
14	20	39	14
15	12	40	11
16	13	41	16
17	9	42	12
18	12	43	10
19	16	44	13
20	14	45	17
21	13	46	15
22	14	47	15
23	10	48	13
24	10	49	13
25	23	50	13

Mean 14.6

S.D. 3.4

Variance 11.8

Range 9 to 23

Individual variation Group (Natural lighting Conditions)

Rat No: 52

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	34	26	33
2	36	27	36
3	38	28	37
4	32	29	46
5	33	30	49
6	38	31	37
7	41	32	31
8	36	33	38
9	39	34	34
10	37	35	34
11	41	36	37
12	37	37	49
13	41	38	41
14	29	39	43
15	38	40	39
16	39	41	38
17	42	42	41
18	43	43	37
19	44	44	38
20	37	45	39
21	37	46	41
22	35	47	38
23	36	48	37
24	39	49	40
25	40	50	37

Mean 38.8

S.D. 3.9

Variance 15.9

Range 29 to 49

Rat No: 53

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	38	26	31
2	32	27	25
3	39	28	24
4	29	29	32
5	45	30	28
6	36	31	34
7	37	32	33
8	33	33	49
9	34	34	38
10	36	35	33
11	36	36	33
12	39	37	30
13	41	38	29
14	39	39	31
15	36	40	34
16	36	41	33
17	36	42	35
18	34	43	31
19	36	44	36
20	27	45	34
21	34	46	32
22	37	47	36
23	31	48	31
24	29	49	36
25	27	50	34

Mean 34.5

S.D. 4.6

Variance 21.2

Range 24 to 49

Individual variation Group (Natural lighting Conditions)

Rat No: 54

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	27	26	28
2	26	27	26
3	17	28	29
4	19	29	26
5	16	30	24
6	32	31	25
7	34	32	23
8	23	33	30
9	30	34	26
10	28	35	28
11	24	36	29
12	33	37	33
13	28	38	27
14	32	39	25
15	21	40	29
16	20	41	27
17	31	42	31
18	27	43	26
19	22	44	29
20	28	45	30
21	23	46	30
22	23	47	29
23	24	48	24
24	29	49	28
25	24	50	31

Mean 27.1

S.D. 4.0

Variance 16.4

Range 16 to 34

Rat No: 55

Time 10.00 - 11.00 hours

Date 20.11.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	26	5
2	3	27	3
3	8	28	5
4	3	29	2
5	4	30	2
6	5	31	8
7	4	32	8
8	5	33	8
9	4	34	4
10	5	35	8
11	5	36	5
12	3	37	4
13	6	38	6
14	9	39	5
15	2	40	9
16	10	41	9
17	9	42	7
18	9	43	4
19	8	44	6
20	7	45	5
21	6	46	4
22	3	47	4
23	10	48	5
24	9	49	5
25	9	50	6

Mean 6.3

S.D. 2.2

Variance 5.1

Range 2 to 10

Individual variation Group (Artificial lighting Conditions)

Rat No: 69

Time 12.00 - 13.00 hours

Date 12.2.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	11	26	12
2	12	27	12
3	12	28	12
4	10	29	7
5	7	30	13
6	12	31	10
7	13	32	7
8	13	33	12
9	11	34	6
10	6	35	14
11	10	36	12
12	6	37	14
13	8	38	9
14	9	39	14
15	9	40	10
16	14	41	12
17	8	42	12
18	8	43	9
19	10	44	11
20	14	45	10
21	13	46	12
22	9	47	11
23	13	48	14
24	12	49	8
25	11	50	7

Mean 11.1

S.D. 2.4

Variance 5.8

Range 6 to 14

Rat No: 74

Time 12.00 - 13.00 hours

Date 12.2.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	13	26	13
2	18	27	11
3	12	28	15
4	11	29	10
5	13	30	10
6	7	31	10
7	12	32	12
8	13	33	6
9	11	34	8
10	9	35	12
11	13	36	9
12	12	37	13
13	14	38	13
14	13	39	14
15	22	40	8
16	13	41	10
17	12	42	9
18	15	43	12
19	14	44	13
20	11	45	12
21	7	46	10
22	10	47	10
23	11	48	10
24	12	49	15
25	14	50	11

Mean 12.3

S.D. 2.7

Variance 7.4

Range 6 to 22

Individual variation Group (Artificial lighting Conditions)

Rat No: 71

Time 12.00 - 13.00 hours

Date 12.2.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	7	26	13
2	15	27	13
3	14	28	11
4	7	29	13
5	14	30	8
6	9	31	11
7	17	32	14
8	18	33	6
9	11	34	7
10	8	35	7
11	10	36	7
12	15	37	9
13	9	38	8
14	9	39	10
15	10	40	15
16	19	41	10
17	16	42	10
18	19	43	12
19	13	44	7
20	17	45	13
21	19	46	16
22	16	47	14
23	16	48	14
24	15	49	10
25	10	50	10

Mean 12.6

S.D. 3.7

Variance 13.7

Range 6 to 19

Rat No: 72

Time 12.00 - 13.00 hours

Date 12.2.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	10	26	8
2	12	27	12
3	10	28	6
4	7	29	12
5	14	30	11
6	13	31	17
7	10	32	6
8	8	33	8
9	11	34	10
10	10	35	11
11	5	36	9
12	5	37	12
13	15	38	11
14	6	39	15
15	10	40	14
16	14	41	14
17	14	42	12
18	8	43	16
19	11	44	11
20	16	45	10
21	11	46	12
22	12	47	11
23	10	48	13
24	8	49	15
25	15	50	8

Mean 11.5

S.D. 2.9

Variance 8.9

Range 5 to 17

Individual variation Group (Artificial lighting Conditions)

Rat No: 70

Time 12.00 - 13.00 hours

Date 12.2.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	7	26	8
2	10	27	12
3	6	28	6
4	6	29	7
5	9	30	10
6	7	31	12
7	10	32	9
8	11	33	8
9	5	34	8
10	11	35	10
11	6	36	7
12	10	37	9
13	11	38	5
14	11	39	13
15	11	40	10
16	10	41	10
17	9	42	15
18	10	43	12
19	11	44	13
20	9	45	9
21	10	46	8
22	8	47	12
23	10	48	13
24	9	49	12
25	7	50	11

Mean 10.0

S.D. 2.2

Variance 5.2

Range 5 to 15

Rat No: 73

Time 12.00 - 13.00 hours

Date 12.2.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	14	26	20
2	17	27	14
3	13	28	12
4	11	29	9
5	14	30	15
6	16	31	16
7	15	32	10
8	18	33	13
9	9	34	23
10	14	35	10
11	15	36	16
12	12	37	17
13	15	38	17
14	12	39	18
15	17	40	16
16	17	41	14
17	16	42	14
18	9	43	9
19	14	44	12
20	12	45	15
21	15	46	12
22	17	47	9
23	15	48	15
24	18	49	16
25	23	50	10

Mean 14.9

S.D. 3.3

Variance 10.9

Range 9 to 23

Control Group

Series I

Rat No: 9

Time 06.00 hours

Skin

Magnification (Linear) 185

Date 3.5.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	40.7	10	12.5	26	34.2	12	17.0
2	39.9	8	10.0	27	40.4	17	21.2
3	39.2	6	7.5	28	41.6	2	2.5
4	37.3	5	7.1	29	44.4	1	1.1
5	42.1	3	3.7	30	34.5	3	4.2
6	38.9	2	2.5	31	30.0	6	9.9
7	37.2	6	8.5	32	37.0	7	9.9
8	27.2	8	16.0	33	29.6	11	18.2
9	30.5	8	13.2	34	56.1	5	4.5
10	34.5	6	8.5	35	36.4	9	12.7
11	36.7	4	5.6	36	31.5	12	19.9
12	33.5	3	4.2	37	39.6	12	15.0
13	41.7	7	8.7	38	30.6	5	8.3
14	44.8	3	3.3	39	40.5	4	5.0
15	37.5	5	6.2	40	39.3	6	7.5
16	40.9	5	6.2	41	33.1	10	14.2
17	53.1	5	4.5	42	33.2	9	12.7
18	41.1	10	12.5	43	30.6	12	19.9
19	41.2	14	17.5	44	39.9	11	13.7
20	41.2	1	1.2	45	30.9	6	9.9
21	38.4	10	12.5	46	43.3	9	9.9
22	44.0	6	6.6	47	37.6	6	7.5
23	50.0	6	6.0	48	40.8	3	3.7
24	33.6	2	2.8	49	35.1	3	4.2
25	39.0	7	8.7	50	36.1	2	2.8

Mean 9.1

S.D. 5.1

Variance 26.9

Range 1.1 to 21.2

Control Group

Series I

Rat No: 4

Time 08.00 hours

Skin

Magnification (Linear) 185

Date 4.3.55

Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	48.7	6	6.0
2	40.7	2	2.5
3	56.7	12	10.8
4	42.5	4	5.0
5	52.1	9	9.0
6	48.3	3	3.0
7	47.6	5	5.0
8	49.0	5	5.0
9	32.0	2	3.3
10	37.9	7	8.7
11	47.0	4	4.4
12	38.2	5	6.2
13	53.4	7	6.3
14	38.0	2	2.5
15	54.5	6	5.4
16	59.6	8	6.6
17	53.7	5	4.5
18	52.0	6	6.0
19	49.5	3	3.0
20	58.1	8	6.6
21	43.0	3	3.3
22	40.5	8	10.0
23	48.7	9	9.0
24	44.0	7	7.7
25	50.5	4	5.0
26	54.6	7	6.3
27	37.2	5	7.1
28	45.5	7	7.7
29	49.6	9	9.0
30	49.2	4	4.0
31	65.0	4	3.0
32	40.5	1	1.2
33	43.0	4	4.4
34	43.5	7	7.7
35	51.5	2	2.0
36	63.8	13	9.8
37	60.0	14	11.6
38	36.1	6	8.5
39	46.4	4	4.4
40	53.0	9	8.1
41	57.5	11	9.1
42	42.2	5	6.2
43	47.4	5	5.5

Mean 6.3

S.D. 2.4

Variance 6.1

Range 1.2 to 11.6

Control Group

Series I

Rat No: 7

Time 10.00 hours

Skin

Magnification (Linear) 185

Date 26.4.55

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	78.0	6	3.7	26	66.6	8	7.2
2	49.4	2	2.0	27	43.3	2	2.2
3	60.0	4	3.3	28	51.3	6	6.0
4	55.0	7	6.3	29	53.2	7	6.3
5	61.4	8	6.6	30	59.3	8	6.6
6	65.0	6	4.5	31	52.6	5	4.5
7	60.8	4	3.3	32	30.0	4	6.6
8	71.8	3	2.1	33	47.1	6	6.6
9	68.7	7	4.9	34	44.5	3	3.3
10	62.6	4	3.0	35	46.4	2	2.2
11	63.6	6	4.5	36	58.6	8	6.6
12	69.2	5	3.5	37	45.2	6	6.6
13	65.0	9	6.8	38	48.4	5	5.0
14	77.0	6	3.9	39	43.5	1	1.1
15	69.4	9	6.3	40	37.1	2	2.8
16	76.0	5	3.3	41	64.3	5	3.8
17	64.8	8	6.0	42	76.5	6	3.9
18	40.0	8	10.0	43	41.9	5	6.2
19	46.7	6	6.6	44	33.8	5	7.1
20	62.0	4	3.3	45	25.6	5	10.0
21	63.7	8	6.0	46	38.2	3	3.7
22	53.5	3	2.7	47	48.0	6	6.0
23	61.3	7	5.8	48	30.9	2	3.3
24	67.6	4	2.8	49	36.5	1	1.4
25	54.1	7	6.3	50	34.7	1	1.4

Mean 4.9

S.D. 2.1

Variance 4.7

Range 1.1 to 10.0

Control Group

Series I

Rat No: 6

Time 12.00 hours

Skin

Magnification (Linear) 185

Date 18.4.55

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	43.7	8	8.8	26	56.8	5	4.5
2	58.4	8	6.6	27	50.3	9	9.0
3	42.7	7	7.7	28	62.8	7	5.3
4	50.8	5	5.0	29	54.1	6	5.4
5	58.0	11	9.1	30	71.4	7	4.9
6	52.8	8	7.2	31	63.3	6	4.5
7	61.4	9	7.4	32	44.1	1	1.1
8	51.8	5	5.0	33	68.2	7	4.9
9	45.7	2	2.2	34	68.2	4	2.8
10	38.7	2	2.5	35	57.5	2	1.6
11	46.1	5	5.5	36	47.2	6	6.6
12	55.1	3	2.7	37	53.3	5	4.5
13	53.1	4	3.6	38	73.6	17	11.2
14	73.0	8	5.2	39	68.4	11	7.8
15	73.6	7	4.6	40	62.0	6	4.9
16	61.0	6	4.9	41	39.2	5	6.2
17	75.0	10	6.6	42	54.3	8	7.2
18	63.0	8	6.0	43	67.6	7	4.9
19	73.4	8	5.2	44	69.7	9	6.3
20	62.5	12	9.9	45	58.3	7	5.8
21	71.0	9	6.3	46	48.4	5	5.0
22	49.5	7	7.0	47	60.4	8	6.6
23	45.3	7	7.7	48	58.5	5	4.1
24	49.5	4	4.0	49	56.5	9	8.1
25	51.4	4	4.0	50	53.7	7	6.3

Mean 5.8

S.D. 2.1

Variance 4.6

Range 1.1 to 11.2

Control Group

Series I

Rat No: 2

Time 14.00 hours

Skin

Magnification (Linear) 185

Date 4.2.55

Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	41.5	7	8.7	26	44.2	13	14.4
2	52.1	19	19.0	27	42.1	10	12.5
3	31.4	6	9.9	28	49.7	9	9.0
4	41.6	8	10.0	29	48.7	7	7.0
5	50.1	2	2.0	30	46.2	11	12.2
6	41.0	9	12.5	31	42.4	8	10.0
7	56.0	13	11.7	32	47.6	12	12.0
8	48.0	11	11.0	33	43.8	8	8.8
9	48.8	7	7.0	34	34.8	11	15.6
10	44.4	11	12.2	35	45.6	9	9.9
11	41.0	12	15.0	36	46.4	10	11.1
12	40.7	8	10.0	37	47.5	8	8.0
13	31.6	7	11.6	38	48.3	9	9.0
14	43.6	14	15.5	39	49.2	8	8.0
15	46.7	10	11.1	40	43.3	10	11.1
16	51.7	11	11.0	41	41.7	7	8.7
17	42.2	9	11.2				
18	47.8	7	7.0				
19	40.2	6	7.5				
20	41.9	5	6.2				
21	41.8	10	12.5				
22	46.7	13	14.4				
23	47.9	12	12.0				
24	48.1	7	7.0				
25	44.6	11	12.2				

Mean 10.9

S.D. 3.0

Variance 9.4

Range 2.0 to 19.0

Control Group

Rat No: 5

Skin

Date 13.4.55

Series I

Time 16.00 hours

Magnification (Linear) 185

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 sq. cm.
1	37.1	2	2.8	26	71.2	5	3.5
2	45.4	1	1.1	27	59.3	5	4.1
3	43.1	1	1.1	28	54.1	2	1.8
4	43.5	2	2.2	29	55.0	4	3.6
5	41.5	2	2.5	30	59.3	3	2.4
6	51.8	1	1.0	31	61.1	6	4.9
7	47.0	2	2.2	32	65.4	3	2.2
8	48.1	4	4.0	33	60.0	0	0.0
9	50.0	1	1.0	34	56.7	4	3.6
10	57.3	3	2.7	35	56.5	6	5.4
11	64.0	4	3.0	36	73.3	3	1.9
12	48.3	1	1.0	37	65.3	1	0.7
13	48.1	2	2.0	38	50.0	3	3.0
14	42.1	3	3.7	39	54.7	1	0.9
15	58.1	2	1.6	40	50.1	5	5.0
16	69.3	4	2.8	41	63.3	3	2.2
17	58.1	2	1.6	42	56.2	8	7.2
18	66.0	6	4.5	43	57.6	1	0.8
19	59.5	4	3.3	44	61.0	3	2.4
20	49.6	0	0.0	45	64.5	3	2.2
21	59.1	1	0.8	46	58.3	2	1.6
22	45.4	2	2.2	47	60.5	2	1.6
23	43.1	2	2.2	48	76.1	3	1.9
24	68.0	2	1.4	49	57.5	4	3.3
25	50.0	2	2.0	50	63.6	3	2.2

Mean 2.6

S.D. 1.4

Variance 2.1

Range 0.0 to 7.2

Control Group

Series I

Rat No: 8

Time 18.00 hours

Skin

Magnification (Linear) 185

Date 25.4.55

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	50.3	0	0.0	26	44.5	1	1.1
2	43.7	0	0.0	27	41.8	1	1.2
3	46.9	1	1.1	28	35.7	2	2.8
4	42.8	1	1.1	29	43.7	2	2.8
5	46.7	2	2.2	30	46.7	0	0.0
6	42.7	2	2.2	31	44.8	1	1.1
7	39.1	2	2.5	32	53.5	3	2.7
8	48.7	2	2.0	33	43.4	0	0.0
9	42.5	2	2.5	34	48.6	3	3.0
10	45.6	2	2.2	35	41.1	4	5.0
11	46.3	0	0.0	36	44.4	3	3.3
12	42.7	0	0.0	37	46.0	2	2.2
13	38.2	1	1.2	38	44.2	1	1.1
14	43.9	0	0.0	39	51.5	2	2.0
15	47.1	0	0.0	40	53.8	4	3.6
16	43.9	1	1.1	41	56.7	1	0.9
17	42.8	0	0.0	42	46.8	2	2.2
18	41.7	1	1.2	43	44.6	0	0.0
19	51.9	2	2.0	44	60.0	2	1.6
20	50.0	3	3.0	45	53.2	2	1.8
21	32.3	4	6.6	46	43.5	2	2.2
22	38.2	2	2.5	47	44.1	3	3.3
23	43.9	0	0.0	48	51.9	1	1.0
24	31.2	1	1.6	49	51.4	2	2.0
25	41.2	1	1.2	50	46.2	4	4.4

Mean 2.1

S.D. 1.4

Variance 2.0

Range 0.0 to 6.6

Control Group

Series I

Rat No: 3

Time 20.00 hours

Skin

Magnification (Linear) 185

Date 16.2.55

Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	53.8	1	0.9	26	52.7	3	2.7
2	58.7	2	1.6	27	69.0	4	3.0
3	54.6	3	2.7	28	50.3	2	2.0
4	47.1	2	2.2	29	47.0	1	1.1
5	58.6	1	0.8	30	45.5	1	1.1
6	52.6	0	0.0	31	47.1	1	1.1
7	70.0	0	0.0	32	48.0	1	1.0
8	51.6	4	4.0	33	49.0	3	3.0
9	50.6	2	2.0	34	53.0	3	2.7
10	68.2	2	1.4	35	60.0	2	1.6
11	63.4	3	2.2	36	62.1	4	3.3
12	64.2	4	3.0	37	47.5	2	2.0
13	51.5	4	4.0	38	46.5	1	1.1
14	40.0	1	1.2	39	42.3	2	2.5
15	42.7	2	2.2	40	45.5	2	2.2
16	55.4	0	0.0	41	48.5	1	1.0
17	57.2	2	1.8	42	52.1	0	0.0
18	62.6	1	0.7	43	46.7	2	2.2
19	49.7	0	0.0	44	47.6	1	1.0
20	45.0	3	3.3	45	42.9	2	2.2
21	50.7	3	3.0	46	39.0	3	3.7
22	50.3	1	1.0	47	41.0	0	0.0
23	49.4	3	3.0	48	56.7	1	0.9
24	43.6	4	4.4	49	54.7	1	0.9
25	61.0	2	1.6	50	48.1	2	2.0

Mean 2.1

S.D. 1.1

Variance 1.4

Range 0.0 to 4.4

Control Group

Series I

Rat No: 1

Time 22.00 hours

Skin

Magnification (Linear) 185

Date 2.12.54

Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	33.4	4	5.9	26	39.0	1	1.2
2	39.4	3	3.8	27	40.7	2	2.4
3	37.8	1	1.3	28	39.0	1	1.2
4	37.7	2	2.6	29	36.0	3	4.1
5	30.0	1	1.6	30	34.6	1	1.4
6	35.0	1	1.4	31	31.7	1	1.5
7	37.5	3	4.0	32	29.9	0	0.0
8	39.4	1	1.2	33	29.0	0	0.0
9	37.2	4	5.3	34	31.0	0	0.0
10	44.0	2	2.2	35	31.6	1	1.5
11	38.0	1	1.3				
12	38.6	1	1.2				
13	49.8	3	3.0				
14	48.8	1	1.0				
15	50.5	2	2.0				
16	46.3	2	2.1				
17	50.5	1	1.0				
18	35.6	3	4.2				
19	41.6	2	2.3				
20	38.8	0	0.0				
21	36.8	1	1.3				
22	36.6	1	1.3				
23	37.4	2	2.6				
24	40.7	1	1.2				
25	39.0	2	2.5				

Mean 2.3

S.D. 1.3

Variance 1.7

Range 0.0 to 5.9

Control Group

Series I

Rat No: 11

Time 24.00 hours

Skin

Magnification (Linear) 185

Date 2.5.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	50.3	6	6.0	26	43.6	1	1.1
2	44.5	1	1.1	27	42.8	2	2.2
3	43.5	2	2.2	28	46.1	4	4.4
4	53.5	2	1.8	29	47.9	3	3.0
5	47.2	4	4.4	30	48.6	2	2.0
6	43.0	0	0.0	31	42.1	1	1.2
7	53.9	2	1.8	32	41.7	3	3.7
8	52.6	6	5.4	33	46.3	4	4.4
9	42.8	3	3.3	34	42.1	2	2.5
10	41.1	2	2.5	35	41.1	1	1.2
11	40.7	4	5.0	36	46.8	2	2.2
12	40.8	3	3.7	37	43.9	2	2.2
13	43.1	3	3.3	38	43.9	3	3.2
14	41.3	2	2.5	39	42.8	1	1.1
15	46.1	1	1.1	40	46.5	2	2.2
16	42.9	0	0.0	41	42.7	4	4.4
17	50.4	4	4.0	42	46.1	5	5.5
18	42.2	3	3.9	43	50.8	3	3.0
19	46.1	2	2.2	44	47.2	6	6.6
20	41.3	1	1.2	45	42.8	5	5.5
21	46.5	3	3.3	46	46.3	6	6.6
22	47.5	3	3.0	47	49.3	4	4.0
23	50.9	2	2.0	48	46.1	3	3.3
24	40.1	1	1.2	49	45.5	7	7.7
25	47.5	1	1.1	50	45.8	6	6.6

Mean 3.4

S.D. 1.7

Variance 2.9

Range 0.0 to 7.7

Control Group

Series I

Rat No: 10

Time 02.00 hours

Skin

Magnification (Linear) 185

Date 3.5.55

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	56.2	0	0.0	26	52.1	0	0.0
2	48.4	1	1.0	27	53.5	1	0.9
3	61.6	2	1.6	28	47.1	0	0.0
4	76.7	2	1.3	29	59.3	0	0.0
5	55.0	1	0.9	30	49.6	0	0.0
6	72.4	1	0.7	31	47.6	1	1.0
7	61.0	3	2.4	32	52.3	0	0.0
8	61.2	2	1.6	33	46.6	2	2.2
9	64.4	2	1.5	34	57.3	2	1.8
10	62.8	0	0.0	35	43.8	2	2.2
11	67.1	1	0.7	36	46.0	1	1.1
12	58.2	1	0.8	37	45.3	2	2.2
13	66.5	2	1.5	38	47.9	0	0.0
14	49.0	3	3.0	39	50.2	0	0.0
15	63.1	1	0.7	40	51.9	0	0.0
16	67.3	2	1.5	41	46.4	0	0.0
17	70.0	1	0.7	42	59.4	2	1.6
18	58.9	0	0.0	43	70.8	2	1.4
19	60.2	0	0.0	44	56.7	1	0.9
20	57.5	1	0.8	45	52.9	0	0.0
21	62.8	0	0.0	46	51.2	2	2.0
22	59.6	0	0.0	47	61.3	0	0.0
23	66.5	3	2.2	48	43.1	1	1.1
24	52.1	2	2.0	49	53.6	1	0.9
25	48.2	1	1.0	50	61.3	0	0.0

Mean 1.2

S.D. 0.7

Variance 0.6

Range 0.0 to 3.0

Control Group

Series I

Rat No: 12

Time 04.00 hours

Skin

Magnification (Linear) 185

Date 3.5.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	51.6	5	5.0	26	51.2	3	3.0
2	52.6	6	5.4	27	43.7	7	7.7
3	43.7	4	4.4	28	41.1	2	2.5
4	56.7	7	6.3	29	46.8	1	1.1
5	53.2	4	3.6	30	48.9	3	3.0
6	60.0	5	4.1	31	43.6	3	3.3
7	50.1	5	5.0	32	43.8	6	6.6
8	42.9	6	6.6	33	42.1	5	6.2
9	59.1	7	5.8	34	41.1	2	2.5
10	46.2	3	3.3	35	41.7	6	7.9
11	53.9	6	5.4	36	46.7	5	5.5
12	53.2	5	4.5	37	42.1	6	7.9
13	43.2	2	2.2	38	43.8	7	7.7
14	40.0	1	1.2	39	40.1	9	11.2
15	58.7	7	5.8	40	43.8	5	5.5
16	53.8	6	5.4	41	42.2	1	1.2
17	54.4	4	3.6	42	46.1	4	4.4
18	46.8	3	3.3	43	42.3	3	3.7
19	43.9	2	2.2	44	56.1	7	6.3
20	61.1	8	6.6	45	57.2	8	7.2
21	48.7	1	1.0	46	42.8	5	5.5
22	52.9	5	4.5	47	42.1	4	5.0
23	56.7	4	3.6	48	55.5	6	5.4
24	53.2	6	5.4	49	50.0	4	4.0
25	52.3	6	6.0	50	58.7	6	4.9

Mean 4.9

S.D. 1.9

Variance 3.8

Range 1.0 to 11.2

Control Group

Series I

Rat No: 9

Time 06.00 hours

Oesophagus

Magnification (Linear) 185

Date 3.5.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	72.5	20	14.2	26	66.0	21	15.9
2	79.6	18	11.1	27	74.3	19	12.5
3	81.0	14	8.6	28	55.2	16	14.4
4	78.2	28	17.5	29	66.6	12	9.1
5	80.5	20	12.4	30	66.6	19	14.4
6	76.4	21	13.8	31	59.2	15	12.4
7	68.4	10	7.1	32	66.7	19	14.4
8	56.6	27	24.5	33	67.2	21	15.9
9	50.5	15	15.0	34	66.3	14	10.6
10	58.8	16	13.2	35	62.2	16	13.2
11	50.5	16	16.0	36	71.3	17	12.0
12	55.7	27	24.5	37	55.8	15	13.5
13	61.5	16	13.2	38	52.2	20	20.0
14	62.5	24	20.0	39	50.0	19	19.0
15	57.2	12	11.7	40	54.5	15	13.5
16	57.3	10	9.0	41	51.6	18	18.0
17	70.5	25	17.8	42	60.2	16	13.2
18	69.2	30	21.1	43	50.7	18	18.0
19	68.5	15	10.6	44	67.0	18	13.6
20	72.3	18	11.8	45	60.9	16	13.2
21	57.9	20	16.6	46	80.0	28	17.5
22	65.0	24	18.4	47	61.5	29	24.1
23	75.2	26	17.3	48	66.7	17	12.9
24	72.5	16	11.3	49	74.5	22	14.5
25	74.2	19	12.5	50	X	X	X

Mean per Unit area 15.0

S.D. 4.0

Variance 16.1

Range . . . . . 7.1 to 24.5

Mean per Section 19.4

S.D. 4.8

Variance 23.9

Range . . . . . 10 to 30

Control Group

Series I

Rat No: 4

Time 08.00 hours

Oesophagus

Magnification (Linear) 185

Date 4.3.55

Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	77.8	27	16.6	26	117.1	21	9.1
2	66.7	16	12.1	27	70.0	20	14.2
3	71.3	12	8.5	28	109.7	27	12.2
4	87.2	11	6.5	29	117.3	21	9.1
5	70.0	45	32.1	30	90.0	17	9.4
6	69.6	32	22.8	31	75.6	12	7.9
7	60.7	22	18.2	32	68.4	30	21.4
8	151.5	58	19.8	33	104.7	22	10.4
9	63.6	22	16.7	34	61.4	18	14.9
10	64.0	27	20.7	35	61.8	39	32.5
11	67.4	25	19.2	36	63.0	29	22.3
12	132.2	62	23.8	37	75.8	10	6.6
13	71.5	28	20.0	38	56.8	20	18.0
14	148.7	55	18.3	39	104.5	24	11.4
15	68.5	24	17.1	40	74.4	25	16.6
16	71.8	42	30.0	41	63.2	32	24.5
17	153.0	48	15.4	42	61.4	22	18.2
18	67.5	31	22.1	43	74.7	9	5.9
19	92.3	37	20.5	44	69.0	26	18.5
20	67.3	32	24.6	45	98.7	29	14.5
21	60.9	29	24.1	46	62.6	32	24.5
22	77.1	13	8.5				
23	110.8	23	10.4				
24	104.5	11	5.2				
25	64.6	11	8.3				

Mean per Unit area 16.6

S.D. 7.0

Variance 50.0

Range . . . . . 5.2 to 32.5

Mean per Section 27.2

S.D. 12.2

Variance 155.8

Range . . . . . 9 to 62

Control Group

Series I

Rat No: 7

Time 10.00 hours

Oesophagus

Magnification (Linear) 185

Date 21.4.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	54.1	21	18.9	26	54.1	20	18.0
2	45.2	18	19.9	27	59.2	18	14.9
3	68.3	18	12.7	28	53.2	19	17.1
4	35.6	13	18.4	29	34.2	11	15.6
5	54.5	15	13.5	30	40.5	16	20.0
6	60.6	18	14.9	31	49.0	16	16.0
7	53.5	16	14.4	32	63.3	17	12.9
8	67.8	23	16.4	33	55.2	25	22.7
9	53.4	24	21.8	34	51.6	21	21.0
10	41.1	15	18.7	35	47.2	18	19.9
11	48.7	16	16.0	36	35.5	13	18.4
12	60.1	24	20.0	37	54.7	27	24.5
13	62.5	28	23.3	38	54.4	24	21.8
14	62.3	20	16.6	39	75.7	24	16.0
15	40.5	13	16.2	40	81.6	26	16.2
16	57.4	23	20.9	41	65.1	20	15.2
17	55.5	14	12.6	42	45.6	21	23.3
18	59.5	19	15.7	43	85.2	24	14.1
19	60.5	21	17.4	44	59.6	19	15.7
20	53.0	15	13.5	45	69.6	28	20.0
21	50.2	21	21.0	46	83.0	26	15.2
22	65.7	22	16.7	47	50.7	18	18.0
23	55.4	20	18.0	48	53.2	18	16.2
24	55.7	14	12.6	49	65.5	22	16.7
25	46.0	13	14.4	50	61.6	35	29.1

Mean per Unit area 17.7

S.D. 3.5

Variance 12.4

Range . . . . . 12.6 to 29.1

Mean per Section 20.6

S.D. 4.4

Variance 20.0

Range . . . . . 11 to 35

Control Group

Series I

Rat No: 6

Time 12.00 hours

Oesophagus

Magnification (Linear) 185

Date 18.4.55

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	61.5	18	14.9	26	30.8	12	19.9
2	44.3	15	16.6	27	31.0	15	24.9
3	62.3	17	14.1	28	34.5	12	17.0
4	56.3	19	17.1	29	31.0	15	24.9
5	58.2	13	10.7	30	63.5	17	12.9
6	62.1	20	16.6	31	67.8	17	12.0
7	79.5	24	15.0	32	71.8	18	12.7
8	46.5	15	16.6	33	61.2	17	14.1
9	48.7	20	20.0	34	85.5	30	17.5
10	55.5	14	12.6	35	83.5	21	12.5
11	50.0	18	18.0	36	44.8	5	5.5
12	50.0	20	20.0	37	42.7	7	7.7
13	34.3	19	26.9	38	56.6	19	17.1
14	28.6	11	18.2	39	27.0	6	12.0
15	49.4	20	20.0	40	53.1	14	12.6
16	62.7	21	15.9	41	50.0	20	20.0
17	29.1	14	23.2	42	30.5	11	18.2
18	55.8	16	14.4	43	50.8	16	16.0
19	45.2	15	16.6	44	30.5	13	21.5
20	84.4	26	15.2	45	55.3	14	12.6
21	50.0	20	20.0	46	28.6	12	19.9
22	26.2	10	20.0	47	27.5	13	21.5
23	53.1	16	14.4	48	28.5	14	23.2
24	30.5	12	19.9	49	31.2	11	18.2
25	31.6	12	19.9	50	81.9	14	8.6

Mean per Unit area 16.8

S.D. 4.4

Variance 20.2

Range . . . . . 5.5 to 26.9

Mean per Section 16.3

S.D. 4.7

Variance 22.3

Range . . . . 5 to 30

Control Group

Series I

Rat No: 2

Time 14.00 hours

Oesophagus

Magnification (Linear) 185

Date 4.2.55

Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	47.6	5	5.2	24	46.2	10	10.8
2	51.3	13	12.6	25	54.4	11	10.0
3	47.8	10	10.4	26	47.2	14	14.8
4	49.3	10	10.1	27	53.8	12	11.1
5	46.2	5	5.4	28	62.3	12	9.6
6	51.4	7	6.8	29	49.3	13	13.1
7	66.5	20	15.0	30	47.1	8	8.4
8	61.4	13	10.5	31	49.3	10	10.1
9	47.8	8	8.3	32	51.0	11	10.7
10	52.6	12	11.4	33	51.2	8	7.8
11	53.1	16	15.0	34	49.4	14	14.1
12	51.9	19	18.0	35	47.0	10	10.6
13	61.1	17	13.9	36	48.4	10	10.3
14	49.7	7	7.0	37	48.4	10	10.3
15	46.1	16	17.3	38	50.0	7	7.0
16	52.2	16	15.3				
17	57.6	14	12.1				
18	64.0	17	13.2				
19	52.0	7	6.7				
20	79.5	17	10.6				
21	53.0	8	7.5				
22	51.7	11	10.6				
23	74.1	19	12.8				

Mean per Unit area 11.1

S.D. 3.2

Variance 10.3

Range . . . . . 5.2 to 18.0

Mean per Section 12.3

S.D. 4.0

Variance 16.0

Range . . . . . 5 to 20

Control Group

Series I

Rat No: 5

Time 16.00 hours

Oesophagus

Magnification (Linear) 185

Date 13.4.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cms.
1	52.0	4	4.0	26	64.4	6	4.5
2	59.5	4	3.3	27	71.4	10	7.1
3	43.7	8	8.8	28	54.3	5	4.5
4	53.4	6	5.4	29	56.0	5	4.5
5	58.7	2	1.6	30	53.6	4	3.6
6	62.0	4	3.3	31	57.4	5	4.5
7	53.3	3	2.7	32	33.5	6	8.5
8	52.1	5	5.0	33	53.0	3	2.7
9	52.2	1	1.0	34	71.3	4	2.8
10	61.0	4	3.3	35	124.1	10	4.1
11	47.2	3	3.3	36	21.6	1	2.5
12	78.2	4	2.4	37	50.4	4	4.0
13	48.5	3	3.0	38	39.5	2	2.5
14	43.2	6	6.6	39	101.7	8	4.0
15	52.3	9	9.0	40	31.4	2	3.3
16	49.4	8	8.0	41	84.1	7	4.3
17	52.3	5	5.0	42	76.4	7	4.6
18	69.4	5	3.5	43	101.0	4	2.0
19	37.6	2	2.5	44	42.5	5	6.2
20	92.3	7	3.8	45	78.5	6	3.7
21	51.1	2	2.0	46	71.1	4	2.8
22	56.3	6	5.4	47	85.9	5	3.1
23	55.7	6	5.4	48	45.4	4	4.4
24	62.1	3	2.4	49	51.5	7	7.0
25	34.1	4	5.6	50	62.5	6	4.9

Mean per Unit area 4.4

S.D. 1.8

Variance 3.6

Range . . . . . 1.0 to 9.0

Mean per Section 5.4

S.D. 2.1

Variance . . . 4.5

Range . . . . . 1 to 10

Control Group — Series I

Rat No: 8 — Time 18.00 hours

Oesophagus — Magnification (Linear) 185

Date 25.4.55

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	47.1	1	1.1	26	61.1	2	1.6
2	51.9	1	1.0	27	114.2	3	1.0
3	56.1	1	0.9	28	102.4	4	2.0
4	53.2	2	1.8	29	44.3	1	1.1
5	47.2	0	0.0	30	53.2	1	0.9
6	48.7	0	0.0	31	54.0	0	0.0
7	47.2	2	2.2	32	46.7	0	0.0
8	51.6	0	0.0	33	51.5	2	2.0
9	47.5	1	1.0	34	49.5	2	2.0
10	41.5	2	2.5	35	53.5	4	3.6
11	51.5	0	0.0	36	106.4	4	1.8
12	59.5	1	0.8	37	112.2	5	2.2
13	52.6	0	0.0	38	113.3	2	0.8
14	50.6	4	4.0	39	53.4	1	0.9
15	48.0	1	1.0	40	45.2	5	5.5
16	40.4	3	3.7	41	121.6	2	0.8
17	41.0	1	1.2	42	53.8	2	1.8
18	41.1	1	1.2	43	51.5	2	2.0
19	54.1	1	0.9	44	102.1	3	1.5
20	42.8	3	3.3	45	120.7	2	0.8
21	91.1	2	1.1	46	50.9	0	0.0
22	74.1	3	1.9	47	54.5	1	0.9
23	41.6	0	0.0	48	57.0	1	0.9
24	98.5	5	2.5	49	56.9	0	0.0
25	41.6	2	2.5	50	55.8	1	0.9

Mean per Unit area 1.6 — Mean per Section 2.3

S.D. . . . . 1.2 — S.D. 1.4

Variance . . . . . 1.5 — Variance 2.0

Range . . . . . 0.0 to 5.5 — Range . . . . . 0 to 5

Control Group

Series I

Rat No: 3

Time 20.00 hours

Oesophagus

Magnification (Linear) 185

Date 16.2.55

Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	46.2	2	2.2	26	47.5	3	3.0
2	56.2	4	3.6	27	55.9	2	1.8
3	63.5	4	3.0	28	46.3	1	1.1
4	59.0	0	0.0	29	48.7	3	3.0
5	52.1	6	6.0	30	49.6	2	2.0
6	62.0	1	0.8	31	47.0	6	6.6
7	65.0	4	3.0	32	59.6	3	2.4
8	43.7	1	1.1	33	57.3	4	3.6
9	61.9	3	2.4	34	48.9	6	6.0
10	57.5	2	1.6	35	51.2	3	3.0
11	42.5	3	3.7	36	43.3	4	4.4
12	57.5	2	1.6	37	60.0	6	4.9
13	49.4	6	6.0	38	63.8	2	1.5
14	64.5	3	2.2	39	62.3	6	4.9
15	45.5	3	3.3	40	57.3	3	2.7
16	59.7	4	3.3	41	66.5	4	3.0
17	56.0	4	3.6	42	58.2	4	3.3
18	58.0	2	1.6	43	57.3	3	2.7
19	65.0	3	2.2	44	59.3	5	4.1
20	50.4	2	2.0	45	48.5	1	1.0
21	63.5	2	1.5	46	50.6	3	3.0
22	50.2	2	2.0	47	52.3	1	1.0
23	45.5	2	2.2	48	60.0	4	3.3
24	48.2	1	1.0	49	49.5	2	2.0
25	60.6	4	3.3	50	50.0	2	2.0

Mean per Unit area 3.0

S.D. 1.4

Variance 2.1

Range . . . . . 0.0 to 6.6

Mean per Section 3.4

S.D. 1.5

Variance 2.3

Range . . . . . 0 to 6

Control Group

Series I

Rat No: 1

Time 22.00 hours

Oesophagus

Magnification (Linear) 185

Date 2.12.54

Serial No: of observations	observed area in Sq. cms.	observed N_o: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of observations	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	61.3	4	3.2	25	57.7	7	6.0
2	61.6	5	4.0	26	57.5	9	7.8
3	57.3	5	4.3	27	58.7	5	4.2
4	60.3	7	5.8	28	62.7	5	3.9
5	61.3	2	1.6	29	62.0	4	3.2
6	58.6	5	4.2	30	68.7	10	7.2
7	60.0	4	3.3	31	59.0	3	2.5
8	62.3	7	5.6	32	58.3	7	6.0
9	59.7	4	3.3	33	53.4	3	2.8
10	61.5	9	7.6	34	59.5	5	4.2
11	63.0	10	7.9	35	57.3	5	4.3
12	58.3	1	0.9	36	59.5	4	3.3
13	58.2	5	4.3	37	53.0	9	8.8
14	54.5	7	6.4	38	62.4	7	5.6
15	57.5	6	5.2	39	61.6	3	2.4
16	55.5	4	3.6	40	59.6	5	4.1
17	55.4	6	5.4	41	53.4	8	7.4
18	63.2	10	7.9	42	53.1	7	6.5
19	65.8	4	3.0	43	61.5	4	3.2
20	65.4	6	4.5	44	61.4	7	5.7
21	67.3	2	1.4				
22	61.6	5	4.0				
23	63.1	7	5.5				
24	57.2	5	4.3				

Mean per Unit area 4.7

S.D. 1.8

Variance 3.3

Range . . . . . 0.9 to 7.9

Mean per Section 6.1

S.D. 2.2

Variance 4.9

Range . . . . . 1 to 10

Control Group

Series I

Rat No: 11

Time 24.00 hours

Oesophagus

Magnification (Linear) 185

Date 2.5.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	81.6	17	10.5	26	58.7	23	19.1
2	65.8	12	9.1	27	46.8	5	5.5
3	52.3	11	11.0	28	65.3	4	3.0
4	78.8	12	7.4	29	47.7	10	10.0
5	73.5	11	7.2	30	53.8	9	8.1
6	60.3	12	9.9	31	57.1	9	8.1
7	61.3	17	14.1	32	66.4	12	9.1
8	76.7	14	9.2	33	67.7	7	5.3
9	75.2	10	6.6	34	53.8	5	4.5
10	62.2	15	12.4	35	83.6	15	8.8
11	66.7	14	10.6	36	66.3	9	6.8
12	61.8	13	10.7	37	62.7	7	5.3
13	58.7	13	10.7	38	84.3	21	12.3
14	61.9	10	8.3	39	92.5	13	7.1
15	45.5	3	3.3	40	52.3	6	6.0
16	44.3	7	7.7	41	62.8	10	7.6
17	44.2	16	17.7	42	82.3	12	7.4
18	45.5	5	5.5	43	94.1	18	9.4
19	45.5	8	8.8	44	55.8	7	6.3
20	48.1	7	7.0	45	45.0	5	5.5
21	47.4	4	4.4	46	54.2	11	9.9
22	44.6	6	6.6	47	52.1	5	5.0
23	44.1	5	5.5	48	66.1	9	6.8
24	56.5	10	9.0	49	54.5	13	11.7
25	50.0	8	8.0	50	58.8	16	13.2

Mean per Unit area 8.6

S.D. 3.2

Variance 10.5

Range . . . . . 3.0 to 19.1

Mean per Section 11.0

S.D. 4.5

Variance 20.8

Range . . . . . 3 to 23

Control Group

Series I

Rat No: 10

Time 02.00 hours

Oesophagus

Magnification (Linear) 185

Date 3.5.55

Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No:	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	41.1	4	5.0	26	101.0	4	2.0
2	49.8	3	3.0	27	103.6	2	0.9
3	67.7	4	2.8	28	93.5	5	2.6
4	68.8	2	1.4	29	95.1	1	0.5
5	45.5	2	2.2	30	104.4	5	2.3
6	52.6	0	0.0	31	101.6	3	1.5
7	45.2	2	2.2	32	88.6	3	1.6
8	44.6	1	1.1	33	84.4	3	1.7
9	54.5	2	1.8	34	101.2	0	0.0
10	37.2	5	7.1	35	98.7	3	1.5
11	70.2	2	1.4	36	95.0	3	1.5
12	47.3	1	1.1	37	96.2	0	0.0
13	63.4	2	1.5	38	86.1	3	1.7
14	97.4	6	3.1	39	93.3	2	1.0
15	45.5	1	1.1	40	99.0	5	2.5
16	105.0	6	2.8	41	83.8	4	2.3
17	72.3	7	4.9	42	84.5	2	1.1
18	69.2	4	2.8	43	94.5	1	0.5
19	102.1	3	1.5	44	103.8	3	1.4
20	106.5	4	1.9	45	103.5	2	0.9
21	92.4	5	2.7	46	99.4	2	1.0
22	107.3	2	0.9	47	109.3	4	1.8
23	97.5	2	1.0	48	89.8	2	1.1
24	103.3	5	2.3	49	78.7	4	2.4
25	100.3	4	2.0	50	103.1	5	2.3

Mean per Unit area 2.0

S.D. 1.3

Variance 1.8

Range . . . . . 0.0 to 7.1

Mean per Section 3.5

S.D. 1.6

Variance 2.6

Range . . . . . 0 to 7

Control Group

Series I

Rat No: 12

Time 04.00 hours

Oesophagus

Magnification (Linear) 185

Date 3.5.55

Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.	Serial No: of Section	observed area in Sq. cms.	observed No: of mitoses	No: of mitoses per 50 Sq. cm.
1	48.6	19	19.0	26	44.5	18	19.9
2	41.8	16	20.0	27	58.1	13	10.7
3	46.4	17	18.8	28	45.5	12	13.3
4	40.4	14	17.5	29	47.5	15	15.0
5	40.0	8	10.0	30	49.6	8	8.0
6	41.1	8	10.0	31	56.1	19	17.1
7	42.6	11	12.2	32	50.7	14	14.0
8	43.2	11	12.2	33	47.0	12	13.3
9	38.7	13	16.2	34	59.0	13	10.7
10	40.0	9	11.2	35	56.3	15	13.5
11	66.5	12	9.1	36	48.4	14	14.0
12	42.3	11	13.7	37	53.9	13	11.7
13	71.4	14	9.9	38	53.2	12	10.8
14	66.6	14	10.6	39	47.1	11	12.2
15	53.1	13	11.7	40	47.8	12	12.0
16	69.4	20	14.2				
17	62.6	21	15.9				
18	67.8	10	7.1				
19	53.2	12	10.8				
20	66.7	20	15.2				
21	43.0	14	15.5				
22	54.2	13	11.7				
23	47.6	13	13.0				
24	53.3	9	8.1				
25	34.3	6	8.5				

Mean per Unit area 13.1

S.D. 3.3

Variance 10.9

Range . . . . . 7.1 to 20.0

Mean per Section 13.7

S.D. 3.5

Variance 12.3

Range . . . . . 6 to 21

Control Group

Series II

Rat No: 23

Time 18.00 hours

Date 10.6.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	21	3
2	4	22	4
3	2	23	4
4	3	24	6
5	2	25	4
6	2	26	1
7	3	27	3
8	4	28	6
9	4	29	9
10	1	30	7
11	1	31	8
12	3	32	2
13	2	33	4
14	2	34	4
15	0	35	4
16	4	36	7
17	7	37	4
18	1	38	5
19	2	39	2
20	2	40	2

Mean 4.1

S.D. 2.0

Variance 4.3

Range 0 to 9

Control Group

Series II

Rat No: 26

Time 24.00 hours

Date 10.6.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	0	21	2
2	3	22	2
3	0	23	1
4	0	24	1
5	3	25	6
6	2	26	2
7	2	27	2
8	3	28	3
9	2	29	7
10	4	30	3
11	5	31	7
12	5	32	3
13	1	33	4
14	2	34	2
15	3	35	3
16	4	36	2
17	3	37	4
18	5	38	3
19	2	39	4
20	3	40	3

Mean 3.4

S.D. 1.6

Variance 2.6

Range 0 to 7

Control Group

Series II

Rat No: 18

Time 02.00 hours

Date 11.8.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	7	26	14
2	7	27	11
3	9	28	13
4	10	29	8
5	12	30	8
6	5	31	15
7	12	32	10
8	9	33	6
9	9	34	17
10	9	35	7
11	6	36	6
12	9	37	13
13	11	38	12
14	11	39	8
15	8	40	9
16	8	41	4
17	7	42	11
18	15	43	8
19	12	44	11
20	13	45	8
21	4	46	11
22	7	47	10
23	8	48	8
24	10	49	19
25	6	50	6

Mean 10.1

S.D. 3.3

Variance 11.4

Range 4 to 19

Control Group

Series II

Rat No: 20

Time 06.00 hours

Date 11.8.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	26	6
2	7	27	3
3	7	28	10
4	4	29	8
5	2	30	9
6	5	31	5
7	5	32	5
8	4	33	5
9	6	34	4
10	7	35	5
11	1	36	4
12	7	37	6
13	7	38	6
14	2	39	9
15	3	40	5
16	9	41	1
17	6	42	10
18	6	43	9
19	8	44	7
20	5	45	7
21	7	46	11
22	6	47	4
23	7		
24	2		
25	8		

Mean 6.4

S.D. 2.3

Variance 5.5

Range 1 to 11

Control Group

Series II

Rat No: 17

Time 10.00 hours

Date 6.8.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	24	26	14
2	34	27	27
3	30	28	24
4	20	29	44
5	19	30	22
6	31	31	36
7	34	32	31
8	31	33	19
9	10	34	26
10	26	35	38
11	24	36	26
12	17	37	28
13	20	38	26
14	24	39	29
15	23	40	37
16	27	41	32
17	25	42	17
18	23	43	16
19	18	44	14
20	23	45	21
21	31	46	16
22	26	47	23
23	18	48	24
24	30	49	16
25	19	50	19

Mean 25.5

S.D. 7.1

Variance 50.8

Range 10 to 44

Control Group

Series II

Rat No: 19

Time 04.00 hours

Date 11.8.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	8	26	6
2	9	27	3
3	7	28	8
4	11	29	4
5	9	30	5
6	10	31	8
7	9	32	6
8	4	33	7
9	7	34	8
10	8	35	9
11	8	36	6
12	5	37	7
13	8	38	7
14	10	39	8
15	5	40	6
16	11	41	14
17	11	42	10
18	6	43	11
19	6	44	9
20	3	45	6
21	8	46	10
22	8	47	15
23	10	48	9
24	2	49	8
25	7	50	6

Mean 8.3

S.D. 2.5

Variance 6.6

Range 2 to 15

Control Group

Series II

Rat No: 13

Time 08.00 hours

Date 14.6.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	15	26	13
2	12	27	14
3	11	28	10
4	31	29	16
5	15	30	12
6	19	31	14
7	26	32	18
8	20	33	10
9	19	34	15
10	19	35	22
11	18	36	18
12	21	37	15
13	15	38	14
14	12	39	18
15	18	40	18
16	18	41	10
17	16	42	17
18	24	43	17
19	15	44	13
20	28	45	18
21	12	46	13
22	12	47	14
23	11	48	11
24	15	49	14
25	18	50	14

Mean 16.7

S.D. 4.5

Variance 20.5

Range 10 to 31

Control Group

Series II

Rat No: 15

Time 14.00 hours

Date 5.8.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	23	26	16
2	18	27	22
3	20	28	22
4	19	29	20
5	22	30	10
6	21	31	19
7	30	32	35
8	28	33	29
9	28	34	20
10	23	35	37
11	11	36	23
12	25	37	38
13	27	38	39
14	19	39	21
15	15	40	37
16	20	41	27
17	19	42	38
18	25	43	26
19	30	44	29
20	29	45	25
21	29	46	17
22	27	47	24
23	24	48	27
24	24	49	20
25	18	50	15

Mean 24.7

S.D. 6.4

Variance 41.6

Range 10 to 39

Control Group

Series II

Rat No: 21

Time 12.00 hours

Date 10.6.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	22	26	31
2	23	27	24
3	18	28	26
4	26	29	22
5	24	30	27
6	32	31	15
7	26	32	18
8	13	33	31
9	23	34	23
10	21	35	25
11	18	36	18
12	29	37	22
13	27	38	15
14	21	39	18
15	33	40	26
16	24	41	26
17	30	42	19
18	25	43	23
19	28	44	20
20	25	45	30
21	22	46	24
22	24	47	26
23	22	48	23
24	30	49	18
25	18	50	26

Mean 22.9

S.D. 4.6

Variance 21.5

Range 13 to 32

Control Group

Series II

Rat No: 22

Time 16.00 hours

Date 10.6.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	29	26	15
2	16	27	16
3	27	28	15
4	27	29	15
5	22	30	16
6	16	31	16
7	27	32	18
8	16	33	12
9	14	34	11
10	18	35	16
11	12	36	11
12	11	37	14
13	14	38	15
14	14	39	19
15	15	40	16
16	12	41	12
17	10	42	17
18	14	43	15
19	19	44	10
20	12	45	7
21	15	46	15
22	11	47	12
23	10	48	10
24	13	49	16
25	16	50	11

Mean 15.8

S.D. 4.6

Variance 21.6

Range 7 to 29

Control Group

Series II

Rat No: 24

Time 20.00 hours

Date 10.6.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	3	21	0
2	1	22	1
3	0	23	1
4	0	24	1
5	2	25	2
6	1	26	0
7	1	27	2
8	3	28	0
9	2	29	1
10	1	30	0
11	1	31	1
12	1	32	0
13	0	33	1
14	2	34	2
15	3	35	1
16	1	36	1
17	1	37	0
18	1	38	1
19	2	39	0
20	1	40	1

Mean 1.5

S.D. 0.8

Variance 0.7

Range 0 to 3

Control Group

Series II

Rat No: 25

Time 22.00 hours

Date 10.6.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	2	21	2
2	3	22	5
3	4	23	1
4	5	24	2
5	1	25	0
6	2	26	3
7	3	27	3
8	1	28	0
9	2	29	1
10	3	30	1
11	3	31	1
12	4	32	1
13	2	33	0
14	3	34	0
15	6	35	1
16	5	36	3
17	7	37	3
18	4	38	3
19	0	39	3
20	3	40	2

Mean 3.0

S.D. 1.7

Variance 2.9

Range 0 to 7

Control Group

Series III

Rat No: 66

Time 04.00 hours

Date 11.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	15	26	14
2	16	27	13
3	16	28	20
4	19	29	26
5	27	30	23
6	16	31	19
7	14	32	23
8	14	33	22
9	19	34	35
10	15	35	16
11	15	36	11
12	16	37	15
13	16	38	21
14	21	39	16
15	20	40	17
16	21	41	10
17	14	42	22
18	28	43	20
19	13	44	19
20	28	45	15
21	21	46	18
22	17	47	20
23	17	48	14
24	17	49	20
25	18	50	20

Mean 18.9

S.D. 4.7

Variance 22.1

Range 10 to 35

Control Group

Series III

Rat No: 67

Time 06.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	14	26	18
2	14	27	15
3	11	28	11
4	14	29	12
5	13	30	12
6	18	31	28
7	13	32	15
8	17	33	24
9	17	34	16
10	10	35	18
11	18	36	18
12	18	37	12
13	14	38	15
14	15	39	21
15	18	40	18
16	22	41	19
17	15	42	19
18	10	43	20
19	18	44	26
20	14	45	19
21	12	46	15
22	16	47	31
23	10	48	11
24	14	49	12
25	13	50	15

Mean 16.7

S.D. 4.5

Variance 20.5

Range 10 to 31

Control Group

Series III

Rat No: 57

Time 10.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	26	26	32
2	35	27	23
3	24	28	28
4	19	29	32
5	21	30	29
6	26	31	26
7	28	32	24
8	26	33	30
9	22	34	26
10	30	35	25
11	33	36	31
12	22	37	22
13	17	38	18
14	30	39	21
15	23	40	25
16	24	41	21
17	21	42	22
18	21	43	17
19	34	44	21
20	30	45	22
21	30	46	34
22	32	47	40
23	27	48	26
24	27	49	26
25	20	50	33

Mean 26.6

S.D. 5.1

Variance 27.0

Range 17 to 40

Control Group

Series III

Rat No: 68

Time 08.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	18	26	31
2	26	27	30
3	18	28	22
4	23	29	24
5	26	30	22
6	24	31	25
7	30	32	28
8	20	33	25
9	23	34	30
10	19	35	24
11	26	36	33
12	26	37	21
13	18	38	27
14	15	39	29
15	22	40	18
16	18	41	21
17	25	42	23
18	23	43	13
19	31	44	26
20	18	45	32
21	15	46	24
22	27	47	26
23	22	48	18
24	26	49	23
25	24	50	22

Mean 22.9

S.D. 4.6

Variance 21.5

Range 13 to 33

Control Group

Series III

Rat No: 58

Time 12.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	11	26	16
2	16	27	13
3	10	28	10
4	12	29	11
5	15	30	15
6	7	31	12
7	10	32	19
8	15	33	14
9	17	34	10
10	12	35	12
11	16	36	15
12	19	37	14
13	15	38	14
14	14	39	11
15	11	40	12
16	16	41	18
17	11	42	14
18	12	43	16
19	18	44	27
20	16	45	16
21	16	46	22
22	15	47	27
23	15	48	27
24	16	49	16
25	15	50	29

Mean 15.7

S.D. 4.6

Variance 21.4

Range 7 to 29

Control Group

Series III

Rat No: 59

Time 14.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	23	26	22
2	25	27	17
3	20	28	19
4	24	29	16
5	18	30	26
6	15	31	20
7	18	32	21
8	30	33	14
9	26	34	17
10	20	35	16
11	21	36	35
12	11	37	25
13	20	38	21
14	19	39	9
15	19	40	15
16	26	41	14
17	23	42	16
18	23	43	12
19	18	44	13
20	22	45	13
21	21	46	15
22	18	47	10
23	17	48	13
24	16	49	10
25	17	50	11

Mean 19.1

S.D. 5.3

Variance 28.6

Range 9 to 35

Control Group

Series III

Rat No: 60

Time 16.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	6	26	9
2	7	27	5
3	3	28	6
4	7	29	4
5	5	30	6
6	7	31	3
7	5	32	5
8	5	33	6
9	8	34	7
10	8	35	10
11	6	36	10
12	11	37	6
13	7	38	4
14	6	39	4
15	5	40	7
16	9	41	8
17	4	42	6
18	8	43	2
19	8	44	8
20	9	45	6
21	12	46	10
22	13	47	9
23	6	48	9
24	4	49	9
25	6	50	13

Mean 7.4

S.D. 2.4

Variance 6.1

Range 2 to 13

Control Group

Series III

Rat No: 61

Time 18.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	8	26	9
2	7	27	5
3	11	28	5
4	4	29	10
5	10	30	7
6	17	31	4
7	10	32	4
8	8	33	4
9	6	34	7
10	9	35	9
11	4	36	10
12	5	37	6
13	6	38	7
14	8	39	13
15	5	40	8
16	7	41	9
17	11	42	4
18	13	43	6
19	12	44	9
20	7	45	7
21	9	46	5
22	8	47	5
23	6	48	2
24	11	49	6
25	10	50	8

Mean 8.2

S.D. 2.8

Variance 8.4

Range 2 to 17

Control Group

Series III

Rat No: 62

Time 20.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	2	26	3
2	2	27	7
3	2	28	8
4	5	29	2
5	2	30	7
6	3	31	2
7	1	32	1
8	5	33	3
9	1	34	5
10	2	35	1
11	4	36	2
12	7	37	3
13	5	38	2
14	4	39	3
15	8	40	2
16	8	41	1
17	4	42	1
18	5	43	3
19	3	44	2
20	1	45	2
21	1	46	5
22	3	47	3
23	1	48	3
24	5	49	2
25	5	50	2

Mean 3.8

S.D. 2.0

Variance 4.2

Range 1 to 8

Control Group

Series III

Rat No: 63

Time 22.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	2	26	3
2	2	27	5
3	3	28	4
4	1	29	5
5	4	30	2
6	1	31	2
7	2	32	5
8	4	33	7
9	3	34	2
10	2	35	2
11	3	36	1
12	3	37	3
13	6	38	2
14	5	39	3
15	1	40	6
16	1	41	4
17	6	42	1
18	0	43	3
19	1	44	0
20	3	45	3
21	5	46	4
22	5	47	1
23	3	48	5
24	3	49	3
25	4	50	1

Mean 3.5

S.D. 1.6.

Variance 2.8

Range 0 to 7

Control Group

Series III

Rat No: 64

Time 24.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	3	26	6
2	3	27	6
3	5	28	2
4	4	29	4
5	5	30	8
6	4	31	8
7	5	32	5
8	8	33	3
9	5	34	8
10	4	35	4
11	7	36	3
12	2	37	1
13	4	38	1
14	6	39	5
15	5	40	4
16	3	41	1
17	4	42	2
18	3	43	6
19	5	44	8
20	7	45	7
21	5	46	6
22	5	47	9
23	14	48	6
24	15	49	8
25	5	50	8

Mean 5.8

S.D. 2.7

Variance 7.8

Range 1 to 15

Control Group

Series III

Rat No: 65

Time 02.00 hours

Date 11.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	3	26	7
2	4	27	2
3	6	28	4
4	3	29	3
5	3	30	1
6	5	31	2
7	2	32	4
8	3	33	3
9	0	34	2
10	4	35	4
11	7	36	2
12	6	37	6
13	4	38	4
14	4	39	1
15	1	40	3
16	5	41	1
17	3	42	2
18	1	43	1
19	2	44	2
20	2	45	5
21	3	46	1
22	0	47	7
23	2	48	2
24	6	49	2
25	10	50	4

Mean 3.8

S.D. 2.0

Variance 4.3

Range 0 to 10

Reversed Group

Series IV

Rat No: 40

Time 06.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	4	26	5
2	5	27	7
3	2	28	6
4	5	29	5
5	2	30	3
6	6	31	8
7	6	32	3
8	3	33	6
9	3	34	4
10	1	35	2
11	8	36	2
12	9	37	2
13	9	38	1
14	5	39	7
15	5	40	1
16	7	41	7
17	3	42	3
18	3	43	3
19	5	44	4
20	8	45	2
21	7	46	9
22	5	47	3
23	3	48	7
24	2	49	4
25	4	50	5

Mean 5.1

S.D. 2.2

Variance 5.1

Range 1 to 9

Reversed Group

Series IV

Rat No: 42

Time 08.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	9	26	4
2	1	27	5
3	8	28	5
4	2	29	3
5	2	30	3
6	4	31	5
7	5	32	4
8	1	33	2
9	6	34	0
10	6	35	4
11	6	36	5
12	2	37	3
13	3	38	3
14	4	39	3
15	1	40	3
16	0	41	5
17	0	42	5
18	3	43	1
19	1	44	3
20	3	45	6
21	6	46	3
22	3	47	1
23	3	48	5
24	2	49	4
25	2	50	2

Mean 3.9

S.D. 2.0

Variance 4.0

Range 0 to 9

Reversed Group

Series IV

Rat No: 32

Time 18.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	13	26	16
2	22	27	8
3	19	28	13
4	21	29	9
5	17	30	9
6	20	31	7
7	13	32	8
8	11	33	10
9	12	34	11
10	12	35	9
11	10	36	12
12	15		
13	22		
14	10		
15	5		
16	13		
17	12		
18	8		
19	7		
20	10		
21	7		
22	8		
23	13		
24	10		
25	16		

Mean 12.3

S.D. 4.1

Variance 17.3

Range 5 to 22

Reversed Group

Series IV

Rat No: 33

Time 20.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	14	26	12
2	20	27	14
3	10	28	15
4	14	29	16
5	18	30	14
6	16	31	17
7	15	32	12
8	27	33	16
9	20	34	13
10	9	35	18
11	6	36	17
12	11		
13	15		
14	14		
15	9		
16	14		
17	11		
18	16		
19	13		
20	18		
21	9		
22	18		
23	12		
24	10		
25	10		

Mean 14.7

S.D. 4.0

Variance 16.1

Range 6 to 27

Reversed Group

Series IV

Rat No: 35

Time 22.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	26	26	18
2	20	27	16
3	11	28	17
4	14	29	24
5	17	30	20
6	16	31	13
7	17	32	15
8	17	33	24
9	18	34	17
10	23	35	24
11	25	36	26
12	13	37	16
13	11	38	9
14	23	39	7
15	23	40	16
16	19	41	33
17	14	42	31
18	26	43	24
19	27	44	17
20	12	45	36
21	19	46	36
22	17	47	22
23	32	48	18
24	26	49	24
25	16	50	22

Mean 20.7

S.D. 6.6

Variance 44.1

Range 7 to 36

Reversed Group

Series IV

Rat No: 36

Time 24.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	19	26	19
2	16	27	30
3	24	28	18
4	23	29	26
5	16	30	31
6	21	31	23
7	14	32	18
8	16	33	23
9	17	34	25
10	32	35	27
11	37	36	23
12	29	37	24
13	26	38	20
14	28	39	17
15	26	40	24
16	38	41	26
17	26	42	10
18	19	43	31
19	31	44	34
20	36	45	31
21	22	46	19
22	44	47	20
23	24	48	30
24	27	49	34
25	14	50	24

Mean 25.2

S.D. 7.0

Variance 49.3

Range 10 to 44

Reversed Group

Series IV

Rat No: 37

Time 02.00 hours

Date 17.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	16	26	24
2	16	27	19
3	28	28	23
4	19	29	18
5	9	30	18
6	17	31	9
7	21	32	7
8	15	33	9
9	13	34	13
10	19	35	26
11	11	36	13
12	26	37	17
13	19	38	11
14	18	39	12
15	13	40	16
16	21	41	24
17	21	42	14
18	18	43	13
19	23	44	19
20	14	45	14
21	26	46	15
22	10	47	15
23	26	48	17
24	15	49	15
25	22	50	16

Mean 17.6

S.D. 5.1

Variance 26.2

Range 7 to 28

Reversed Group

Series IV

Rat No: 39

Time 04.00 hours

Date 17.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	26	6
2	4	27	2
3	1	28	5
4	3	29	5
5	1	30	3
6	0	31	2
7	5	32	5
8	3	33	3
9	4	34	1
10	5	35	1
11	4	36	3
12	4	37	0
13	5	38	3
14	3	39	6
15	5	40	7
16	9	41	4
17	5	42	3
18	4	43	1
19	6	44	6
20	5	45	3
21	7	46	6
22	5	47	1
23	7	48	7
24	2	49	3
25	4	50	4

Mean 4.5

S.D. 2.0

Variance 4.0

Range 0 to 9

Reversed Group

Series IV

Rat No: 29

Time 14.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	26	4
2	4	27	2
3	5	28	3
4	4	29	1
5	4	30	2
6	8	31	4
7	10	32	3
8	6	33	7
9	5	34	3
10	8	35	4
11	2	36	4
12	1	37	8
13	3	38	6
14	3	39	7
15	2	40	1
16	0	41	7
17	2	42	3
18	1	43	10
19	2	44	5
20	1	45	7
21	3	46	5
22	1	47	7
23	3	48	4
24	2	49	7
25	3	50	9

Mean 4.8

S.D. 2.5

Variance 6.6

Range 0 to 10

Reversed Group

Series IV

Rat No: 30

Time 16.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	4	26	3
2	3	27	8
3	9	28	1
4	9	29	3
5	5	30	1
6	8	31	6
7	5	32	3
8	4	33	9
9	13	34	4
10	4	35	4
11	5	36	7
12	6	37	6
13	4	38	9
14	1	39	3
15	8	40	7
16	1	41	4
17	7	42	6
18	5	43	8
19	5	44	4
20	6	45	4
21	2	46	1
22	3	47	3
23	7	48	3
24	6	49	6
25	5	50	2

Mean 5.5

S.D. 2.5

Variance 6.6

Range 1 to 13

Reversed Group

Series IV

Rat No: 27

Time 10.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	3	26	3
2	6	27	8
3	2	28	2
4	2	29	2
5	6	30	3
6	1	31	2
7	2	32	1
8	4	33	4
9	7	34	3
10	2	35	1
11	4	36	5
12	2	37	3
13	11	38	0
14	5	39	0
15	6	40	5
16	0	41	4
17	3	42	5
18	2	43	3
19	4	44	5
20	2	45	2
21	2	46	1
22	5	47	3
23	4	48	1
24	3	49	5
25	3	50	6

Mean 3.9

S.D. 2.1

Variance 4.7

Range 0 to 11

Reversed Group

Series IV

Rat No: 28

Time 12.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	2	26	0
2	2	27	4
3	2	28	2
4	1	29	2
5	4	30	3
6	5	31	3
7	3	32	2
8	4	33	3
9	2	34	1
10	3	35	4
11	6	36	5
12	8	37	1
13	4	38	2
14	1	39	6
15	3	40	4
16	5	41	3
17	0	42	4
18	3	43	4
19	2	44	0
20	3	45	2
21	2	46	2
22	5	47	1
23	3	48	3
24	1	49	1
25	1	50	5

Mean 3.4

S.D. 1.7

Variance 3.0

Range 0 to 8

Reversed Group

Series V

Rat No: 43

Time 10.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	0	26	6
2	1	27	5
3	6	28	0
4	7	29	2
5	1	30	3
6	5	31	1
7	4	32	4
8	3	33	3
9	1	34	5
10	6	35	5
11	3	36	1
12	5	37	2
13	2	38	5
14	2	39	2
15	5	40	3
16	8	41	1
17	3	42	2
18	1	43	2
19	3	44	6
20	2	45	1
21	3	46	2
22	3	47	7
23	4	48	5
24	3	49	4
25	2	50	4

Mean 3.8

S.D. 1.9

Variance 3.9

Range 0 to 8

Reversed Group

Series V

Rat No: 44

Time 14.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	4	26	2
2	7	27	2
3	1	28	3
4	3	29	4
5	2	30	4
6	5	31	2
7	2	32	6
8	1	33	2
9	4	34	1
10	0	35	5
11	4	36	0
12	5	37	7
13	4	38	3
14	4	39	3
15	3	40	0
16	4	41	4
17	2	42	1
18	4	43	1
19	5	44	4
20	4	45	3
21	6	46	4
22	5	47	1
23	2	48	0
24	6	49	2
25	3	50	3

Mean 3.7

S.D. 1.8

Variance 3.4

Range 0 to 7

Reversed Group

Series V

Rat No: 31

Time 18.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	15	26	18
2	20	27	24
3	27	28	24
4	24	29	27
5	17	30	29
6	25	31	29
7	29	32	30
8	26	33	25
9	38	34	19
10	27	35	20
11	37	36	15
12	21	37	19
13	39	38	27
14	38	39	25
15	23	40	11
16	37	41	23
17	20	42	28
18	29	43	28
19	35	44	30
20	19	45	21
21	10	46	22
22	20	47	19
23	22	48	20
24	22	49	18
25	16	50	23

Mean 24.7

S.D. 6.7

Variance 45.8

Range 10 to 39

Reversed Group

Series V

Rat No: 34

Time 22.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	29	26	32
2	31	27	34
3	27	28	26
4	30	29	30
5	26	30	35
6	19	31	30
7	27	32	26
8	25	33	30
9	14	34	27
10	18	35	22
11	19	36	17
12	27	37	23
13	29	38	36
14	35	39	25
15	14	40	24
16	33	41	33
17	25	42	17
18	29	43	32
19	20	44	33
20	29	45	39
21	20	46	27
22	16	47	31
23	18	48	23
24	25	49	26
25	25	50	19

Mean 26.5

S.D. 6.0

Variance 36.6

Range 14 to 39

Reversed Group

Series V

Rat No: 38

Time 02.00 hours

Date 17.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	25	26	12
2	19	27	9
3	24	28	18
4	10	29	13
5	15	30	15
6	17	31	21
7	11	32	15
8	19	33	25
9	15	34	20
10	18	35	13
11	21	36	13
12	21	37	24
13	19	38	11
14	33	39	15
15	20	40	16
16	20	41	20
17	27	42	22
18	19	43	25
19	23	44	21
20	11	45	15
21	15	46	18
22	13	47	20
23	21	48	17
24	25	49	22
25	11	50	19

Mean 18.8

S.D. 5.0

Variance 25.5

Range 9 to 33

Reversed Group

Series V

Rat No: 41

Time 06.00 hours

Date 16.9.55

Serial No: of Section...A

No: of Mitoses observed,..B

A	B	A	B
1	8	19	5
2	9	20	10
3	8	21	12
4	8	22	9
5	6	23	10
6	6	24	7
7	11	25	6
8	12	26	11
9	12	27	8
10	8	28	10
11	7	29	8
12	1	30	8
13	8	31	7
14	12	32	7
15	8	33	8
16	14	34	6
17	11	35	8
18	9	36	9

Mean 9.0

S.D. 2.4

Variance 6.1

Range 1 to 14

Foetus

Rat No: F7

Time 06.00 hours

Date 16.12.55

	Foetus Number					
	1	2	3	4	5	6
Serial No: of Sections	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.
1	3	1	2	6	2	7
2	3	2	1	2	2	0
3	5	2	0	1	1	3
4	0	0	3	1	2	1
5	3	4	2	0	6	4
6	6	4	1	4	1	9
7	3	0	3	0	3	0
8	2	1	7	6	0	4
9	2	8	0	5	3	1
10	1	4	1	0	5	1
11	4	1	2	3	1	2
12	1	1	2	0	5	5
13	1	0	2	2	3	0
14	2	0	1	3	2	2
15	0	2	1	1	0	1
16	4	2	3	4	0	0
17	0	2	0	3	3	1
18	3	4	2	2	4	1
19	3	2	2	3	2	2
20	5	3	1	3	1	3
21	2	1	2	2	2	1
22	2	1	1	3	2	5
23	2	4	2	6	1	0
24	4	2	2	0	2	5
25	2	2	1	2	1	3

Mean 2.8

S.D. 1.8

Variance 3.5

Range 0 to 9

Foetus

Rat No: F6

Time 09.00 hours

Date 10.12.55

	Foetus Number					
	1	2	3	4	5	6
Serial No: of Sections	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.
1	5	4	2	4	2	6
2	5	0	5	3	3	2
3	0	1	3	2	2	2
4	3	3	0	1	3	1
5	3	9	1	3	4	3
6	2	5	0	2	4	3
7	2	3	1	4	4	6
8	3	3	3	0	3	0
9	0	2	1	1	3	5
10	4	3	1	0	0	2
11	1	1	1	2	3	5
12	2	5	2	8	1	2
13	3	2	2	4	3	6
14	2	3	5	2	6	2
15	3	5	1	1	2	3
16	1	5	2	5	10	4
17	3	3	1	4	2	3
18	4	3	5	4	1	1
19	7	2	1	0	0	1
20	2	2	3	7	5	3
21	2	3	2	2	3	3
22	2	3	0	1	2	1
23	1	2	1	4	4	1
24	0	5	2	0	3	1
25	2	2	0	1	1	2

Mean 3.2

S.D. 1.9

Variance 3.7

Range 0 to 10

Foetus

Rat No: F1

Time 12.00 hours

Date 15.9.55

	Foetus Number					
Serial No: of Sections	1 No: of M.F.	2 No: of M.F.	3 No: of M.F.	4 No: of M.F.	5 No: of M.F.	6 No: of M.F.
1	6	5	3	7	1	3
2	2	3	5	3	1	4
3	4	4	2	1	6	4
4	1	1	2	2	5	3
5	1	3	2	2	1	4
6	5	2	0	2	0	4
7	1	1	3	2	1	5
8	4	4	2	2	3	3
9	5	2	1	2	2	1
10	3	3	1	3	2	2
11	4	3	2	1	2	4
12	3	2	4	3	3	3
13	3	4	4	7	1	1
14	3	3	0	2	0	5
15	1	0	1	1	2	3
16	0	7	2	4	2	3
17	2	5	6	3	2	0
18	3	5	5	4	2	1
19	1	7	3	2	1	3
20	2	3	7	2	2	5
21	0	3	4	2	3	2
22	0	5	4	2	4	4
23	5	2	2	4	0	2
24	6	3	2	2	2	4
25	5	2	4	2	2	1

Mean 3.3

S.D. 1.6

Variance 2.7

Range 0 to 7

Foetus

Rat No: F3

Time 15.00 hours

Date 6.7.55

	Foetus Number					
	1	2	3	4	5	6
Serial No: of Sections	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.
1	1	4	4	5	7	2
2	1	6	1	3	3	2
3	1	4	2	6	2	5
4	6	0	3	4	2	5
5	4	2	1	5	3	3
6	2	2	6	2	4	1
7	1	0	4	2	4	3
8	2	2	5	0	4	5
9	3	3	3	4	2	3
10	2	2	2	2	4	4
11	4	3	4	8	3	2
12	5	3	1	0	3	4
13	6	6	2	2	2	3
14	2	4	3	0	4	2
15	3	2	7	2	2	3
16	3	6	2	4	2	4
17	3	4	3	5	4	5
18	0	4	3	6	1	9
19	3	4	3	5	0	3
20	2	7	2	1	4	4
21	2	4	2	2	9	6
22	3	2	4	5	4	4
23	1	9	3	1	5	3
24	2	4	1	0	7	2
25	2	3	2	4	3	5

Mean 3.8

S.D. 1.8

Variance 3.6

Range 0 to 9

Foetus

Rat No: F4

Time 18.00 hours

Date 9.9.55

	Foetus Number					
	1	2	3	4	5	6
Serial No: of Sections	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.
1	3	1	0	1	1	1
2	4	1	2	3	4	2
3	2	1	1	4	4	6
4	3	0	2	2	7	2
5	3	3	2	2	1	5
6	1	2	1	4	2	2
7	1	1	1	2	4	3
8	3	3	2	1	7	2
9	3	2	2	0	5	2
10	2	0	2	3	3	3
11	2	4	3	1	2	1
12	0	4	2	0	4	4
13	0	3	2	1	4	6
14	2	2	0	0	3	4
15	3	4	4	5	0	3
16	2	6	2	1	4	0
17	1	2	4	4	4	2
18	1	2	3	0	3	0
19	3	4	1	0	3	0
20	3	4	3	2	3	3
21	2	1	3	1	0	1
22	1	3	3	1	3	3
23	2	3	1	3	6	3
24	2	6	6	5	3	1
25	2	1	1	3	4	2

Mean 3.0

S.D. 1.6

Variance 2.6

Range 0 to 7

Foetus

Rat No: F5

Time 21.00 hours

Date 11.1.56

	Foetus Number			
Serial No: of Sections	1 No: of M.F.	2 No: of M.F.	3 No: of M.F.	4 No: of M.F.
1	4	4	0	7
2	5	3	3	4
3	2	3	6	6
4	3	6	7	6
5	4	1	4	2
6	1	4	4	3
7	1	7	4	2
8	6	7	3	2
9	3	3	5	5
10	3	1	6	3
11	5	4	6	2
12	6	6	5	1
13	5	3	3	2
14	3	6	5	4
15	2	3	6	6
16	3	3	3	5
17	3	3	5	3
18	2	4	6	2
19	8	4	3	1
20	1	6	4	2
21	3	3	5	3
22	2	3	10	2
23	4	4	4	3
24	1	3	6	3
25	2	4	2	2

Mean 4.3

S.D. 1.8

Variance 3.4

Range 0 to 10

Foetus

Rat No: F2

Time 24.00 hours

Date 7.8.55

	Foetus Number					
	1	2	3	4	5	6
Serial No: of Sections	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.
1	6	3	3	0	1	3
2	2	2	3	3	2	2
3	2	0	2	6	3	5
4	4	3	3	4	3	6
5	5	2	1	4	4	2
6	3	2	2	3	1	7
7	3	3	1	6	2	4
8	2	1	1	4	1	4
9	8	6	2	6	3	3
10	4	2	4	4	5	5
11	3	0	3	5	2	4
12	5	2	4	3	1	4
13	6	5	3	2	5	3
14	0	3	2	0	1	4
15	3	6	3	6	2	6
16	1	2	2	2	1	0
17	1	2	5	2	4	6
18	5	1	3	6	3	3
19	3	9	4	2	3	3
20	4	2	4	3	2	4
21	3	4	1	1	3	4
22	1	3	4	2	4	3
23	4	1	2	2	5	2
24	1	2	5	2	3	5
25	4	4	3	1	1	1

Mean 3.6

S.D. 1.6

Variance 2.8

Range 0 to 9

Foetus

Rat No: F8

Time 03.00 hours

Date 20.1.56

	Foetus Number					
	1	2	3	4	5	6
Serial No: of Sections	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.	No: of M.F.
1	6	3	1	4	0	3
2	5	2	4	2	1	2
3	4	0	2	6	2	3
4	3	1	1	0	2	1
5	7	3	3	4	3	1
6	1	2	1	3	0	2
7	5	3	2	1	0	2
8	1	2	2	4	2	2
9	2	1	1	3	3	1
10	1	0	0	0	0	2
11	0	1	0	0	2	1
12	3	1	3	7	2	2
13	3	2	6	0	0	4
14	3	2	1	4	1	4
15	4	3	3	1	1	1
16	2	1	1	1	2	2
17	1	0	1	2	1	4
18	2	1	5	1	1	1
19	1	0	2	4	1	5
20	2	2	4	3	3	2
21	0	0	3	0	2	6
22	2	1	1	3	0	0
23	2	2	1	7	3	3
24	4	2	2	5	0	4
25	3	1	1	4	0	4

Mean 2.7

S.D. 1.6

Variance 2.8

Range 0 to 7

Mother of Foetus

Rat No: F2

Time 24.00 hours

Date 7.8.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	26	6
2	4	27	3
3	2	28	8
4	10	29	8
5	4	30	7
6	7	31	5
7	5	32	6
8	4	33	3
9	3	34	7
10	7	35	4
11	6	36	8
12	3	37	9
13	11	38	5
14	8	39	3
15	7	40	6
16	4	41	8
17	3	42	4
18	8	43	8
19	6	44	7
20	1	45	3
21	4		
22	3		
23	9		
24	9		
25	3		

Mean 6.2

S.D. 2.3

Variance 5.7

Range 1 to 11

Mother of Foetus

Rat No: F3

Time 15.00 hours

Date 6.7.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	7	26	10
2	12	27	13
3	10	28	12
4	9	29	11
5	13	30	8
6	14	31	4
7	16	32	5
8	7	33	5
9	5	34	18
10	14	35	12
11	10	36	9
12	10	37	7
13	10	38	10
14	4	39	8
15	9	40	8
16	12	41	10
17	5	42	6
18	5	43	5
19	9	44	8
20	9	45	13
21	14	46	10
22	8	47	7
23	9	48	9
24	9	49	12
25	8	50	11

Mean 9.9

S.D. 3.1

Variance 9.9

Range 4 to 18

Mother of Foetus

Rat No: F4

Time 18.00 hours

Date 9.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	3	26	5
2	2	27	3
3	2	28	3
4	1	29	3
5	1	30	1
6	0	31	1
7	1	32	1
8	1	33	2
9	2	34	2
10	4	35	4
11	2	36	2
12	0	37	3
13	2	38	1
14	4	39	2
15	7	40	1
16	2	41	1
17	2	42	2
18	0	43	2
19	1	44	2
20	2	45	1
21	3	46	3
22	2	47	1
23	1	48	3
24	2		
25	4		

Mean 2.6

S.D. 1.3

Variance 1.7

Range 0 to 7

Mother of Foetus

Rat No: F5

Time 21.00 hours

Date 11.1.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	9	26	6
2	4	27	7
3	2	28	7
4	4	29	5
5	2	30	6
6	6	31	2
7	3	32	3
8	2	33	3
9	6	34	4
10	3	35	3
11	5	36	7
12	3	37	6
13	3	38	6
14	5	39	5
15	1	40	3
16	7	41	3
17	6	42	5
18	4	43	0
19	4	44	4
20	5	45	3
21	4	46	4
22	4	47	8
23	4	48	3
24	2	49	4
25	2	50	4

Mean 4.7

S.D. 1.8

Variance 3.3

Range 1 to 9

Mother of Foetus

Rat No: F1

Time 12.00 hours

Date 15.9.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	10	26	14
2	10	27	11
3	12	28	10
4	8	29	16
5	15	30	8
6	7	31	7
7	16	32	8
8	16	33	15
9	7	34	7
10	15	35	14
11	11	36	12
12	6	37	17
13	9	38	9
14	17	39	12
15	15	40	12
16	18	41	16
17	15	42	12
18	8	43	9
19	17	44	8
20	10	45	13
21	9	46	16
22	15	47	7
23	16	48	11
24	17	49	12
25	7	50	9

Mean 12.4

S.D. 3.5

Variance 12.6

Range 6 to 18

Mother of Foetus

Rat No: F7

Time 06.00 hours

Date 16.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	5	26	8
2	7	27	6
3	7	28	3
4	4	29	1
5	4	30	10
6	2	31	9
7	5	32	7
8	5	33	7
9	4	34	11
10	6	35	4
11	7	36	4
12	1	37	5
13	7	38	4
14	7	39	6
15	2	40	6
16	3	41	9
17	9	42	5
18	6	43	10
19	6	44	8
20	8	45	9
21	5	46	5
22	7	47	5
23	6	48	5
24	7		
25	2		

Mean 6.4

S.D. 2.3

Variance 5.3

Range 1 to 11

Mother of Foetus

Rat No: F6

Time 09.00 hours

Date 10.12.55

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	10	26	19
2	10	27	11
3	17	28	12
4	15	29	7
5	9	30	15
6	10	31	17
7	10	32	14
8	11	33	9
9	7	34	16
10	11	35	17
11	12	36	11
12	7	37	12
13	10	38	14
14	6	39	12
15	9	40	11
16	11	41	14
17	7	42	14
18	22	43	8
19	18	44	9
20	12	45	10
21	13	46	10
22	11	47	11
23	11	48	8
24	11	49	4
25	15	50	10

Mean 12.1

S.D. 3.5

Variance 12.7

Range 6 to 22

Mother of Foetus

Rat No: F8

Time 03.00 hours

Date 20.1.56

Serial No: of Section...A

No: of Mitoses observed...B

A	B	A	B
1	0	26	2
2	0	27	2
3	1	28	0
4	1	29	0
5	0	30	0
6	2	31	1
7	1	32	2
8	1	33	5
9	1	34	1
10	2	35	1
11	1	36	0
12	4	37	1
13	1	38	1
14	1	39	0
15	2	40	0
16	0	41	2
17	0	42	0
18	1	43	1
19	0	44	2
20	1	45	2
21	1	46	2
22	1	47	1
23	1	48	0
24	0	49	0
25	2	50	1

Mean 1.6

S.D. 1.0

Variance 1.2

Range 0 to 5